

Support Information

Visible Light-Mediated Deoxygenation Protocol for Synthesis of Dipeptide, Amide and Ester without Racemization

Ji-Wei Ren, Qing-Long Tan,* Jian Zuo, Yan-Fei Miao, Pan Zhang, Jing-Hui Sun, and Yin-Feng Han**

Table of Contents

1. General experimental information	2
2. Experimental procedures and characterization data	3
2.1. Optimization studies	3
2.2. General procedure for the synthesis of dipeptides 3	5
2.3. General procedure for the synthesis of chiral amides 5	11
2.4. General procedure for the synthesis of chiral esters 7	12
2.5. Synthetic procedure of 5 mmol scale model reaction	14
2.6. Experimental set-up	15
2.7. UV/Vis Absorption Experiments	15
2.8. Mechanistic experiments	16
2.9. Experiment supporting catalyst regeneration mechanism	16
3. NMR Spectra	18

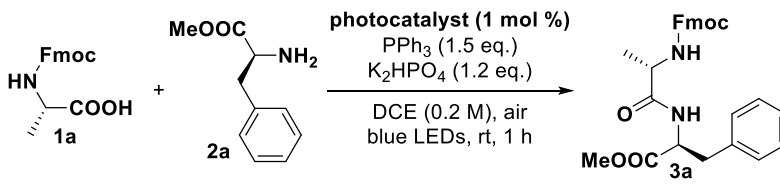
1. General experimental information

Unless otherwise noted, all the substrates and reagents were purchased from commercial suppliers and used without further purification, which were known compounds. ^1H NMR spectra were recorded at 500 MHz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration. ^{13}C NMR data were collected at 125 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. High resolution mass spectroscopy (HRMS) was performed on Thermo Q Exactive Plus (FTMS ESI) mass spectrometer and acetonitrile was used to dissolve the sample. Column chromatography was carried out on silica gel (200-300 mesh).

2. Experimental procedures and characterization data

2.1. Optimization studies

Table S1. The effects of photocatalyst^a

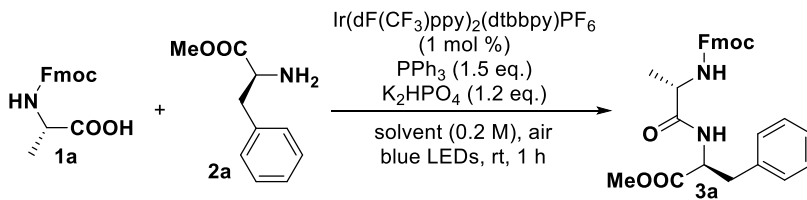


Entry	Photocatalyst	Yield (%) ^b
1	Ru(bpy) ₃ (PF ₆) ₂	trace
2	Ru(bpz) ₃ (PF ₆) ₂	trace
3	Ir(ppy) ₂ (dtbbpy)PF ₆	trace
4	Ir(dF(CF ₃)ppy) ₂ (bpy)PF ₆	58
5	Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆	87
6	<i>fac</i> -Ir(ppy) ₃	trace
7	Rose Bengal	trace
8	Eosin Y	trace
9	Rhodamine B	trace
10	DCA	trace

^aUnless otherwise noted, all reactions were carried out using amino acid **1a** (0.2 mmol, 1.0 equiv.), amino acid ester **2a** (0.24 mmol, 1.2 equiv.), photocatalyst (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and K₂HPO₄ (0.24 mmol, 1.2 equiv.) in 1,2-dichloroethane (1.0 mL) at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W).

^bIsolated yield with >20:1 *dr* determined by ¹H NMR.

Table S2. The effects of solvent^a

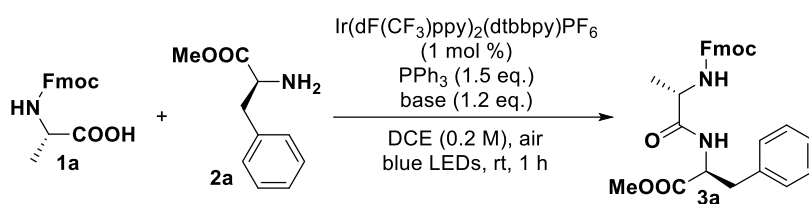


Entry	Solvent	Yield (%) ^b
1	DCE	87
2	MeCN	47
3	DMF	68
4	EtOH	NR

5	THF	40
6	toluene	trace
7	1,4-dioxane	trace

^aUnless otherwise noted, all reactions were carried out using amino acid **1a** (0.2 mmol, 1.0 equiv.), amino acid ester **2a** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and K₂HPO₄ (0.24 mmol, 1.2 equiv.) in solvent (1.0 mL) at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). ^bIsolated yield with >20:1 *dr* determined by ¹H NMR.

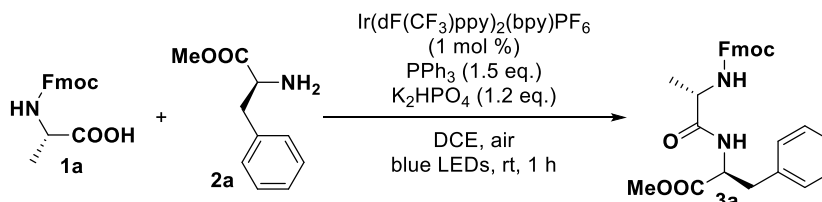
Table S3. The effects of base^a



Entry	Base	Yield (%) ^b
1	K₂HPO₄	87
2	-	50
3	NaHCO ₃	39
4	Na ₂ CO ₃	41
5	K ₂ CO ₃	51

^aUnless otherwise noted, all reactions were carried out using amino acid **1a** (0.2 mmol, 1.0 equiv.), amino acid ester **2a** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and base (0.24 mmol, 1.2 equiv.) in 1,2-dichloroethane (1.0 mL) at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). ^bIsolated yield with >20:1 *dr* determined by ¹H NMR.

Table S4. The effects of concentration^a



Entry	Concentration	Yield (%) ^b
1	0.1	76
2	0.5	85

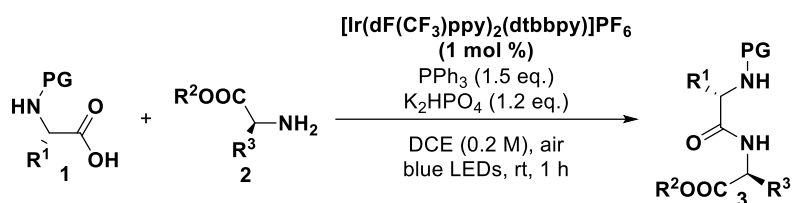
^aUnless otherwise noted, all reactions were carried out using amino acid **1a** (0.2 mmol, 1.0 equiv.), amino acid ester **2a** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and K₂HPO₄ (0.24 mmol, 1.2 equiv.) in 1,2-dichloroethane at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). ^bIsolated yield with >20:1 *dr* determined by ¹H NMR.

Table S5. Control experiments^a

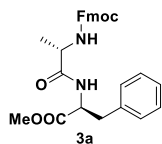
Entry	Variation from the standard conditions	Yield (%) ^b
1	5 mol % of Ir(dF(CF ₃)ppy) ₂ (dtbbpy)PF ₆	88
2	no photocatalyst	NR
3	in dark	NR
4	no PPh ₃	NR

^aUnless otherwise noted, all reactions were carried out using amino acid **1a** (0.2 mmol, 1.0 equiv.), amino acid ester **2a** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and K₂HPO₄ (0.24 mmol, 1.2 equiv.) in 1,2-dichloroethane (1.0 mL) at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). ^bIsolated yield with >20:1 *dr* determined by ¹H NMR.

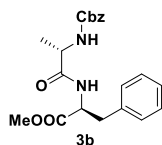
2.2. General procedure for the synthesis of dipeptides **3**



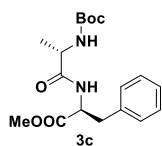
N-protected amino acids **1** (0.2 mmol, 1.0 equiv.), amino acid esters **2** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and K₂HPO₄ (0.24 mmol, 1.2 equiv.) were well mixed in 1,2-dichloroethane (1.0 mL). The resulting mixture was stirred at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). The reaction mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (EtOAc/PE = 20%-40%) to yield dipeptides **3**.



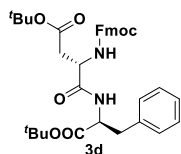
Dipeptide 3a¹: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (82.4 mg, 87% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.77 (d, J = 7.5 Hz, 2H), 7.59 (d, J = 7.5 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.31 (td, J = 7.5, 0.5 Hz, 2H), 7.23 (t, J = 7.5 Hz, 2H), 7.17-7.20 (m, 1H), 7.07 (d, J = 7.5 Hz, 2H), 6.42 (d, J = 6.5 Hz, 1H), 5.30 (d, J = 6.0 Hz, 1H), 4.84-4.88 (m, 1H), 4.38-4.42 (m, 1H), 4.32-4.36 (m, 1H), 4.19-4.24 (m, 2H), 3.72 (s, 3H), 3.15 (dd, J = 14.0, 5.5 Hz, 1H), 3.07 (dd, J = 14.0, 6.5 Hz, 1H), 1.35 (d, J = 6.5 Hz, 3H).



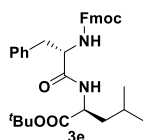
Dipeptide 3b²: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (62.1 mg, 81% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.30-7.38 (m, 5H), 7.21-7.28 (m, 3H), 7.08 (d, J = 7.0 Hz, 2H), 6.44 (d, J = 4.5 Hz, 1H), 5.23 (d, J = 4.5 Hz, 1H), 5.06-5.13 (m, 2H), 4.83-4.87 (m, 1H), 4.20-4.23 (m, 1H), 3.72 (s, 3H), 3.15 (dd, J = 14.0, 6.0 Hz, 1H), 3.07 (dd, J = 14.0, 6.0 Hz, 1H), 1.33 (d, J = 7.0 Hz, 3H).



Dipeptide 3c³: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (55.4 mg, 79% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.22-7.30 (m, 3H), 7.09-7.11 (m, 2H), 6.52 (d, J = 7.5 Hz, 1H), 4.93 (*br s*, 1H), 4.83-4.87 (m, 1H), 4.14 (*br s*, 1H), 3.71 (s, 3H), 3.16 (dd, J = 14.0, 6.0 Hz, 1H), 3.10 (dd, J = 14.0, 6.0 Hz, 1H), 1.44 (s, 9H), 1.31 (d, J = 7.0 Hz, 3H).

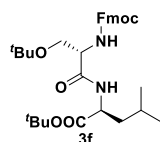


Dipeptide 3d⁴: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (109.8 mg, 89% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, J = 7.5 Hz, 2H), 7.57 (d, J = 7.5 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.29-7.32 (m, 2H), 7.24-7.27 (m, 2H), 7.18-7.21 (m, 3H), 7.02 (d, J = 7.0 Hz, 1H), 5.95 (d, J = 8.0 Hz, 1H), 4.66-4.70 (m, 1H), 4.54 (d, J = 3.0 Hz, 1H), 4.32-4.41 (m, 2H), 4.21 (t, J = 7.0 Hz, 1H), 3.08 (d, J = 6.0 Hz, 2H), 2.90 (dd, J = 17.0, 4.0 Hz, 1H), 2.62 (dd, J = 17.0, 6.5 Hz, 1H), 1.44 (s, 9H), 1.37 (s, 9H).

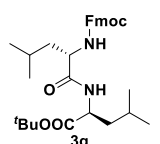


Dipeptide 3e⁴: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (100.2 mg, 90% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.77 (d, J = 7.5 Hz,

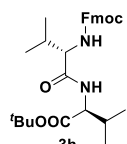
2H), 7.54 (t, $J = 7.0$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 2H), 7.27 (d, $J = 9.0$ Hz, 2H), 7.21-7.24 (m, 1H), 7.18 (d, $J = 5.0$ Hz, 2H), 6.15 (d, $J = 6.5$ Hz, 1H), 5.33 (d, $J = 6.5$ Hz, 1H), 4.42-4.46 (m, 3H), 4.30-4.33 (m, 1H), 4.19 (t, $J = 6.5$ Hz, 1H), 3.03-3.14 (m, 2H), 1.52-1.56 (m, 2H), 1.42-1.46 (m, 10H), 0.90 (d, $J = 6.0$ Hz, 3H), 0.88 (d, $J = 6.0$ Hz, 3H).



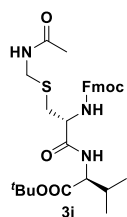
Dipeptide 3f⁴: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (88.4 mg, 80% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.59-7.62 (m, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.30-7.33 (m, 2H), 7.22 (d, $J = 6.5$ Hz, 1H), 5.78 (d, $J = 4.5$ Hz, 1H), 4.47-4.48 (m, 1H), 4.37-4.43 (m, 2H), 4.22-4.25 (m, 2H), 3.83 (dd, $J = 8.5, 3.5$ Hz, 1H), 3.40 (t, $J = 8.5$ Hz, 1H), 1.67-1.71 (m, 1H), 1.60-1.65 (m, 1H), 1.50-1.55 (m, 1H), 1.46 (s, 9H), 1.23 (s, 9H), 0.95 (d, $J = 6.5$ Hz, 6H).



Dipeptide 3g⁴: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (88.9 mg, 85% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.58 (d, $J = 7.5$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.31 (tt, $J = 7.5, 1.0$ Hz, 2H), 6.28 (d, $J = 8.0$ Hz, 1H), 5.26 (d, $J = 8.0$ Hz, 1H), 4.45-4.50 (m, 1H), 4.35-4.43 (m, 2H), 4.21 (t, $J = 7.0$ Hz, 2H), 1.50-1.67 (m, 6H), 1.45 (s, 9H), 0.95 (d, $J = 3.0$ Hz, 6H), 0.91 (dd, $J = 6.0, 2.0$ Hz, 6H).

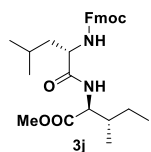


Dipeptide 3h⁴: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (81.4 mg, 82% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.60 (d, $J = 7.0$ Hz, 2H), 7.39 (t, $J = 7.5$ Hz, 2H), 7.29-7.32 (m, 2H), 6.28 (d, $J = 8.5$ Hz, 1H), 5.46 (d, $J = 8.5$ Hz, 1H), 4.41-4.44 (m, 2H), 4.35-4.38 (m, 1H), 4.23 (t, $J = 7.0$ Hz, 1H), 4.05 (t, $J = 7.5$ Hz, 1H), 2.11-2.17 (m, 2H), 1.46 (s, 9H), 0.97 (t, $J = 8.0$ Hz, 6H), 0.91 (dd, $J = 10.0, 7.0$ Hz, 6H).

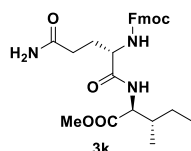


Dipeptide 3i⁵: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); Colorless oil (89.8 mg, 79% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.61 (d, $J = 7.5$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 2H), 7.18 (d, $J = 8.5$ Hz, 1H), 6.66 (br s, 1H), 5.97 (d, $J = 8.0$ Hz, 1H), 4.78 (dd, $J = 14.0, 7.5$ Hz, 1H), 4.68 (dd, $J = 12.5, 7.5$ Hz, 1H), 4.35-4.41 (m, 3H), 4.22-4.26 (m, 2H), 3.01

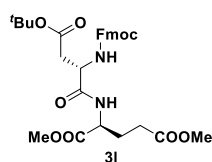
(dd, $J = 14.5, 4.5$ Hz, 1H), 2.73 (dd, $J = 14.5, 8.0$ Hz, 1H), 2.18-2.26 (m, 1H), 2.05 (s, 3H), 1.46 (s, 9H), 0.97 (t, $J = 7.5$ Hz, 6H).



Dipeptide 3j: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (88.4 mg, 92% yield, >20:1 dr); m.p. 120-121 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.74 (d, $J = 7.5$ Hz, 2H), 7.57 (d, $J = 6.5$ Hz, 2H), 7.38 (t, $J = 7.5$ Hz, 2H), 7.28 (td, $J = 7.5, 1.0$ Hz, 2H), 6.71 (d, $J = 8.5$ Hz, 1H), 5.49 (d, $J = 8.5$ Hz, 1H), 4.58 (dd, $J = 8.5, 5.0$ Hz, 1H), 4.34-4.42 (m, 2H), 4.29-4.31 (m, 1H), 4.20 (t, $J = 7.0$ Hz, 1H), 3.70 (s, 3H), 1.88 (br s, 1H), 1.63-1.71 (m, 2H), 1.54-1.57 (m, 1H), 1.38-1.42 (m, 1H), 1.13-1.19 (m, 1H), 0.94 (s, 6H), 0.85-0.88 (m, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 172.2(2), 172.1(9), 156.3, 143.9, 143.8, 141.3, 127.8, 127.1, 125.1, 120.0(1), 119.9(9), 67.1, 56.5, 53.5, 52.1, 47.1, 41.5, 37.8, 25.2, 24.7, 22.9, 22.1, 15.4, 11.6; HRMS (FTMS-ESI) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{28}\text{H}_{36}\text{N}_2\text{NaO}_5^+$ 503.2516, found 503.2526.

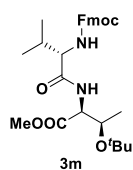


Dipeptide 3k: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (85.9 mg, 87% yield, >20:1 dr); m.p. 210-211 °C; ^1H NMR (500 MHz, CD_3OD) δ 7.80 (d, $J = 7.5$ Hz, 2H), 7.67 (t, $J = 7.5$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.32 (t, $J = 7.5$ Hz, 2H), 4.33-4.42 (m, 3H), 4.21-4.26 (m, 2H), 3.72 (s, 3H), 2.35 (t, $J = 7.5$ Hz, 2H), 2.05-2.12 (m, 1H), 1.88-1.96 (m, 2H), 1.45-1.51 (m, 1H), 1.22-1.36 (m, 2H), 0.90-0.94 (m, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 176.5, 173.1, 172.1, 157.0, 143.9, 143.8, 141.2, 127.4, 126.8(0), 126.7(8), 124.9, 124.8, 119.5, 66.6, 56.9, 54.2, 51.1, 47.0, 37.0, 31.1, 27.7, 24.9, 14.6, 10.4; HRMS (FTMS-ESI) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{33}\text{N}_3\text{NaO}_6^+$ 518.2262, found 518.2252.

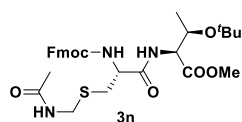


Dipeptide 3l: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (102.4 mg, 90% yield, >20:1 dr); m.p. 104-105 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.61 (d, $J = 6.0$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.32 (t, $J = 7.5$ Hz, 2H), 7.21 (d, $J = 7.5$ Hz, 1H), 6.00 (d, $J = 8.5$ Hz, 1H), 4.57-4.62 (m, 2H), 4.40-4.46 (m, 2H), 4.24 (t, $J = 7.5$ Hz, 1H), 3.73 (s, 3H), 3.64 (s, 3H), 2.97 (dd, $J = 17.0, 3.5$ Hz, 1H), 2.60 (dd, $J = 17.0, 6.0$ Hz, 1H), 2.35-2.45 (m, 2H), 2.20-2.27 (m, 1H), 1.96-2.03 (m, 1H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 173.2, 171.8, 171.4, 170.6, 156.0, 143.8, 143.7, 141.3, 127.8, 127.1, 125.1, 120.0, 82.0, 67.3, 52.6, 51.9, 51.8, 51.1, 47.1, 37.5, 29.9, 28.0, 27.2; HRMS (FTMS-

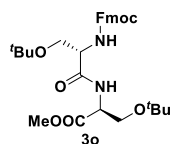
ESI) m/z : $[M+Na]^+$ calcd for $C_{30}H_{36}N_2NaO_9^+$ 591.2313, found 591.2310.



Dipeptide 3m: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); Colorless oil (84.8 mg, 83% yield, >20:1 dr); 1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.60 (d, $J = 7.5$ Hz, 2H), 7.39 (t, $J = 7.5$ Hz, 2H), 7.31 (td, $J = 7.5$, 1.0 Hz, 2H), 6.49 (d, $J = 9.0$ Hz, 1H), 5.57 (d, $J = 9.0$ Hz, 1H), 4.50 (dd, $J = 9.0$, 1.5 Hz, 1H), 4.40-4.44 (m, 1H), 4.34-4.38 (m, 1H), 4.22-4.27 (m, 2H), 4.14-4.17 (m, 1H), 3.71 (s, 3H), 2.12-2.19 (m, 1H), 1.17 (d, $J = 6.0$ Hz, 3H), 1.11 (s, 9H), 1.02 (dd, $J = 13.0$, 6.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 171.0, 156.3, 144.0, 143.9, 141.3, 127.7, 127.1, 125.2, 125.1, 119.9(9), 119.9(7), 74.3, 67.3, 67.1, 60.1, 57.9, 52.2, 47.2, 31.8, 28.3, 21.1, 18.9, 17.8; HRMS (FTMS-ESI) m/z : $[M+Na]^+$ calcd for $C_{29}H_{38}N_2NaO_6^+$ 533.2622, found 533.2628.

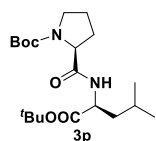


Dipeptide 3n: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); Colorless oil (98.5 mg, 84% yield, >20:1 dr); 1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.61 (dd, $J = 7.5$, 4.0 Hz, 2H), 7.39 (t, $J = 7.5$ Hz, 2H), 7.35 (d, $J = 9.0$ Hz, 1H), 7.31 (t, $J = 7.5$ Hz, 2H), 7.03 (*br s*, 1H), 6.10 (d, $J = 7.5$ Hz, 1H), 4.61-4.64 (m, 2H), 4.47 (dd, $J = 9.0$, 1.5 Hz, 1H), 4.36-4.43 (m, 2H), 4.33 (dd, $J = 14.0$, 6.0 Hz, 1H), 4.23-4.28 (m, 2H), 3.71 (s, 3H), 3.03 (dd, $J = 14.5$, 6.0 Hz, 1H), 2.84 (dd, $J = 14.5$, 6.0 Hz, 1H), 2.02 (s, 3H), 1.20 (d, $J = 6.0$ Hz, 3H), 1.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1(3), 171.0(5), 170.8, 156.4, 143.8, 143.7, 141.3(1), 141.2(9), 127.8, 127.1, 125.2, 120.0, 74.3, 67.4, 67.1, 58.4, 53.8, 52.3, 47.1, 40.6, 34.1, 28.3, 23.2, 21.2; HRMS (FTMS-ESI) m/z : $[M+Na]^+$ calcd for $C_{30}H_{39}N_3NaO_7S^+$ 608.2401, found 608.2408.

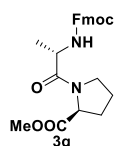


Dipeptide 3o: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); Colorless oil (98.6 mg, 91% yield, >20:1 dr); 1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.69 (d, $J = 7.5$ Hz, 1H), 7.60-7.62 (m, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.31 (td, $J = 7.5$, 1.0 Hz, 2H), 5.86 (d, $J = 4.5$ Hz, 1H), 4.71-4.74 (m, 1H), 4.38 (d, $J = 7.5$ Hz, 2H), 4.30 (*br s*, 1H), 4.24 (t, $J = 7.0$ Hz, 1H), 3.86 (dd, $J = 9.0$, 3.0 Hz, 1H), 3.81 (dd, $J = 8.5$, 4.0 Hz, 1H), 3.74 (s, 3H), 3.56 (dd, $J = 9.0$, 3.0 Hz, 1H), 3.45 (t, $J = 8.5$ Hz, 1H), 1.26 (s, 9H), 1.14 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5(3), 170.4(5), 156.0, 144.0, 143.8, 141.3(1), 141.3(0), 127.7, 127.1, 125.2, 120.0, 74.4, 73.6, 67.1,

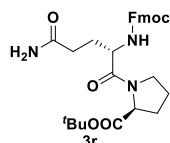
62.0, 61.8, 54.0, 53.2, 52.3, 47.2, 27.4, 27.3; HRMS (FTMS-ESI) m/z : $[M+H]^+$ calcd for $C_{30}H_{41}N_2O_7^+$ 541.2908, found 541.2900.



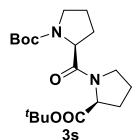
Dipeptide 3p³: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (70.5 mg, 92% yield, >20:1 dr); 1H NMR (500 MHz, $CDCl_3$) δ 6.47-7.23 (m, 1H), 4.22-4.50 (m, 2H), 3.33-3.48 (m, 2H), 2.14-2.33 (m, 2H), 1.87 (*br s*, 2H), 1.57-1.62 (m, 2H), 1.46 (s, 19H), 0.93 (d, $J = 4.0$ Hz, 6H).



Dipeptide 3q¹: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); Colorless oil (69.5 mg, 82% yield, >20:1 dr); 1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, $J = 7.5$ Hz, 2H), 7.59 (dd, $J = 7.5, 1.5$ Hz, 2H), 7.39 (t, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 2H), 5.72 (d, $J = 8.0$ Hz, 1H), 4.51-4.57 (m, 2H), 4.34-4.35 (m, 2H), 4.21 (t, $J = 7.5$ Hz, 1H), 3.68-3.74 (m, 4H), 3.59-3.65 (m, 1H), 2.20-2.28 (m, 1H), 1.97-2.12 (m, 3H), 1.42 (d, $J = 7.0$ Hz, 3H).

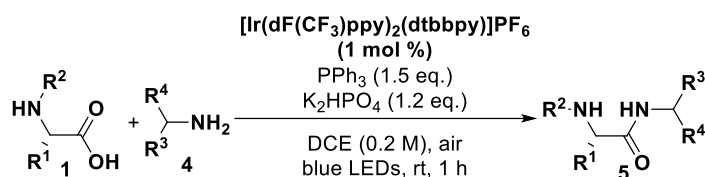


Dipeptide 3r: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); Colorless oil (80.6 mg, 77% yield, >20:1 dr); 1H NMR (500 MHz, CD_3OD) δ 7.80 (d, $J = 8.0$ Hz, 2H), 7.67 (t, $J = 7.0$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.30-7.33 (m, 2H), 4.47 (dd, $J = 9.0, 5.0$ Hz, 1H), 4.32-4.39 (m, 3H), 4.21 (t, $J = 6.5$ Hz, 1H), 3.73-3.82 (m, 2H), 2.35-2.42 (m, 2H), 2.19-2.26 (m, 1H), 2.09-2.15 (m, 1H), 1.98-2.06 (m, 2H), 1.82-1.97 (m, 3H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD) δ 176.3, 171.5, 171.4, 157.1, 143.9, 143.8, 141.2, 127.4, 126.8, 124.9, 124.8, 119.5, 81.4, 66.6, 60.0, 52.0, 47.0, 46.9, 30.6, 28.7, 26.9, 26.8, 24.4; HRMS (FTMS-ESI) m/z : $[M+H]^+$ calcd for $C_{29}H_{36}N_3O_6^+$ 522.2599, found 522.2588.

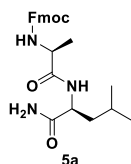


Dipeptide 3s: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); Colorless oil (59.0 mg, 80% yield, >20:1 dr); 1H NMR (500 MHz, $CDCl_3$) δ 4.36-4.50 (m, 2H), 3.55-3.77 (m, 3H), 3.36-3.48 (m, 1H), 2.08-2.21 (m, 3H), 1.80-2.02 (m, 5H), 1.45 (s, 9H), 1.41 (d, $J = 26.0$ Hz, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 171.3, 170.8, 154.5, 153.8, 81.2, 81.0, 79.4, 79.4, 59.5, 57.7(4), 57.6(9), 46.8, 46.6, 46.5(1), 46.4(6), 30.0, 29.1, 28.9, 28.8, 28.5, 28.3, 28.0, 24.9, 24.8, 24.0, 23.6; HRMS (FTMS-ESI) m/z : $[M+H]^+$ calcd for $C_{19}H_{33}N_2O_5^+$ 369.2384, found 369.2392.

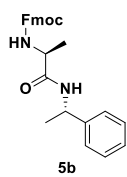
2.3. General procedure for the synthesis of chiral amides **5**



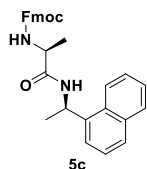
N-protected amino acids **1** (0.2 mmol, 1.0 equiv.), chiral amines **4** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and K₂HPO₄ (0.24 mmol, 1.2 equiv.) were well mixed in 1,2-dichloroethane (1.0 mL). The resulting mixture was stirred at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). The reaction mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (EtOAc/PE = 20%-40%) to yield chiral amides **5**.



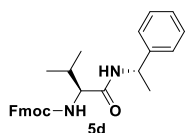
Chiral amide 5a: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (71.2 mg, 84% yield, >20:1 dr); m.p. 91-92 °C; ¹H NMR (500 MHz, CD₃OD) δ 7.66 (d, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 2H), 4.30 (dd, *J* = 8.0, 6.5 Hz, 1H), 4.24 (d, *J* = 7.0 Hz, 2H), 4.08 (t, *J* = 7.0 Hz, 1H), 4.03 (q, *J* = 7.0 Hz, 1H), 1.54-1.59 (m, 1H), 1.49-1.52 (m, 2H), 1.23 (d, *J* = 7.0 Hz, 3H), 0.81 (d, *J* = 6.5 Hz, 3H), 0.78 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (125 MHz, CD₃OD) δ 176.1, 174.2, 157.2, 144.0, 143.8, 141.2, 127.4, 126.8, 124.8(3), 124.8(0), 119.6, 66.6, 51.4, 50.9, 47.0, 40.5, 24.6, 22.2, 20.5, 16.6; HRMS (FTMS-ESI) *m/z*: [M+H]⁺ calcd for C₂₄H₃₀N₃O₄⁺ 424.2231, found 424.2221.



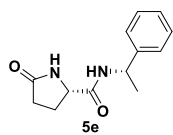
Chiral amide 5b: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (76.3 mg, 92% yield, >20:1 dr); m.p. 176-177 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.20-7.30 (m, 7H), 6.55 (d, *J* = 5.5 Hz, 1H), 5.56 (d, *J* = 6.5 Hz, 1H), 5.05-5.11 (m, 1H), 4.34 (d, *J* = 6.5 Hz, 2H), 4.27-4.28 (m, 1H), 4.16-4.19 (m, 1H), 1.44 (d, *J* = 7.0 Hz, 3H), 1.35 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 171.3, 156.1, 143.7, 143.0, 141.3, 128.7, 127.8, 127.4, 127.1, 126.0, 125.0(7), 125.0(5), 120.0, 67.1, 50.5, 48.9, 47.1, 21.9, 18.9; HRMS (FTMS-ESI) *m/z*: [M+Na]⁺ calcd for C₂₆H₂₆N₂NaO₃⁺ 437.1836, found 437.1822.



Chiral amide 5c: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (87.1 mg, 94% yield, >20:1 dr); m.p. 213-214 °C; ^1H NMR (500 MHz, CDCl_3) δ 8.00 (d, J = 8.5 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.74 (d, J = 7.5 Hz, 2H), 7.70 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.5 Hz, 2H), 7.43 (d, J = 7.0 Hz, 2H), 7.38 (t, J = 7.5 Hz, 3H), 7.33 (t, J = 7.5 Hz, 1H), 7.26 (t, J = 7.5 Hz, 2H), 6.55 (d, J = 5.5 Hz, 1H), 5.82-5.87 (m, 1H), 5.37 (d, J = 6.0 Hz, 1H), 4.17-4.24 (m, 3H), 4.06 (t, J = 7.0 Hz, 1H), 1.62 (d, J = 7.0 Hz, 3H), 1.38 (d, J = 5.5 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.0, 156.0, 143.8, 143.7, 141.3(0), 141.2(8), 138.0, 133.9, 131.0, 128.8, 128.4, 127.8, 127.1, 126.5, 125.8, 125.2, 125.0, 123.2, 122.5, 120.0, 67.1, 50.5, 47.1, 44.9, 20.8, 18.5; HRMS (FTMS-ESI) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{30}\text{H}_{28}\text{N}_2\text{NaO}_3^+$ 487.1992, found 487.1973.

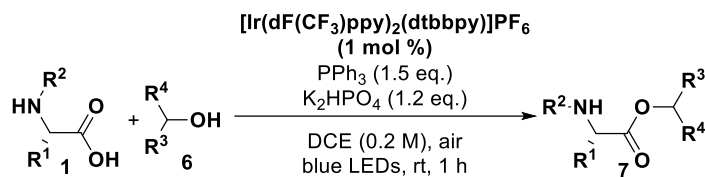


Chiral amide 5d: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); White solid (75.1 mg, 85% yield, >20:1 dr); m.p. 180-181 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.76 (d, J = 7.5 Hz, 2H), 7.55-7.58 (m, 2H), 7.39 (t, J = 7.0 Hz, 2H), 7.30-7.31 (m, 6H), 7.22-7.26 (m, 1H), 6.19 (d, J = 6.5 Hz, 1H), 5.46 (d, J = 8.5 Hz, 1H), 5.08-5.14 (m, 1H), 4.39-4.43 (m, 1H), 4.33-4.36 (m, 1H), 4.17-4.22 (m, 1H), 3.94 (t, J = 7.0 Hz, 1H), 2.03-2.09 (m, 1H), 1.47 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 6.0 Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 170.3, 156.5, 143.8(3), 143.7(8), 142.9, 141.3, 128.7(3), 128.6(8), 127.8, 127.5, 127.1, 126.1, 125.1(1), 125.0(5), 120.0, 67.1, 60.6, 49.0, 47.2, 31.3, 21.7, 19.2, 18.0; HRMS (FTMS-ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{31}\text{N}_2\text{O}_3^+$ 443.2329, found 443.2352.

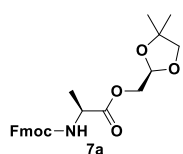


Chiral amide 5e: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-40% (v/v); Colorless oil (37.6 mg, 81% yield, >20:1 dr); ^1H NMR (500 MHz, CDCl_3) δ 7.29-7.34 (m, 4H), 7.24-7.27 (m, 1H), 6.85 (s, 1H), 6.77 (d, J = 7.5 Hz, 1H), 5.07-5.13 (m, 1H), 4.08 (dd, J = 9.0, 5.0 Hz, 1H), 2.44-2.51 (m, 1H), 2.24-2.33 (m, 2H), 2.11-2.18 (m, 1H), 1.48 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 179.4, 171.1, 142.8, 128.7, 127.5, 126.3, 57.1, 49.0, 29.3, 25.8, 21.6; HRMS (FTMS-ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}_2^+$ 233.1285, found 233.1284.

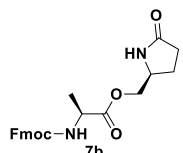
2.4. General procedure for the synthesis of chiral esters 7



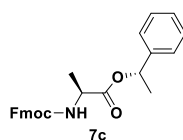
N-protected amino acids **1** (0.2 mmol, 1.0 equiv.), chiral alcohols **6** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and K₂HPO₄ (0.24 mmol, 1.2 equiv.) were well mixed in 1,2-dichloroethane (1.0 mL). The resulting mixture was stirred at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). The reaction mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (EtOAc/PE = 20%-30%) to yield chiral esters **7**.



Chiral ester 7a: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-30% (v/v); Colorless oil (76.5 mg, 90% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 6.5 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 5.43 (d, *J* = 7.5 Hz, 1H), 4.35-4.45 (m, 3H), 4.28-4.32 (m, 1H), 4.17-4.22 (m, 3H), 4.03-4.06 (m, 1H), 3.71-3.74 (m, 1H), 1.44 (d, *J* = 7.0 Hz, 3H), 1.42 (s, 3H), 1.34 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 172.9, 155.7, 143.9, 143.8, 141.3, 127.8, 127.1, 125.1, 120.0, 109.9, 73.4, 67.0, 66.2, 65.5, 49.7, 47.2, 26.7, 25.3, 18.6; HRMS (FTMS-ESI) *m/z*: [M+Na]⁺ calcd for C₂₄H₂₇NNaO₆⁺ 448.1731, found 448.1721.

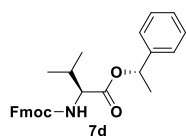


Chiral ester 7b: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-30% (v/v); Colorless oil (76.1 mg, 93% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.77 (*br s*, 1H), 7.74 (d, *J* = 7.5 Hz, 2H), 7.58-7.60 (m, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 2H), 6.21 (d, *J* = 8.0 Hz, 1H), 4.39-4.48 (m, 2H), 4.32-4.36 (m, 2H), 4.22 (t, *J* = 7.0 Hz, 1H), 3.92-3.94 (m, 1H), 3.80 (t, *J* = 9.8 Hz, 1H), 2.28-2.40 (m, 2H), 2.14-2.22 (m, 1H), 1.62-1.69 (m, 1H), 1.44 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 179.0, 172.6, 156.1, 143.9, 143.8, 141.3, 127.7, 127.0(9), 127.0(8), 125.2, 125.1, 120.0(3), 120.0(2), 68.0, 66.9, 52.9, 50.0, 47.2, 29.8, 22.8, 18.5; HRMS (FTMS-ESI) *m/z*: [M+Na]⁺ calcd for C₂₃H₂₄N₂NaO₅⁺ 431.1577, found 431.1575.

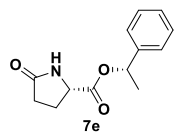


Chiral ester 7c: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-30% (v/v); Colorless oil (73.1 mg, 88% yield, >20:1 dr); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, *J* =

7.5 Hz, 2H), 7.58-7.60 (m, 2H), 7.39 (t, $J = 7.5$ Hz, 2H), 7.27-7.36 (m, 7H), 5.91 (q, $J = 6.5$ Hz, 1H), 5.35 (d, $J = 7.5$ Hz, 1H), 4.34-4.46 (m, 3H), 4.21 (t, $J = 7.0$ Hz, 1H), 1.57 (d, $J = 6.5$ Hz, 3H), 1.39 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 172.3, 155.7, 144.0, 143.8, 141.3, 141.2, 128.6, 128.1, 127.8, 127.1, 126.0, 125.2, 125.1, 120.0, 73.8, 67.1, 49.7, 47.2, 22.3, 18.6; HRMS (FTMS-ESI) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{26}\text{H}_{25}\text{NNaO}_4^+$ 438.1676, found 438.1674.

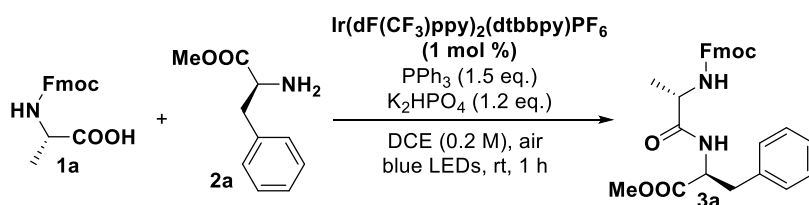


Chiral ester 7d: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-30% (v/v); Colorless oil (80.1 mg, 90% yield, >20:1 dr); ^1H NMR (500 MHz, CDCl_3) δ 7.74 (d, $J = 8.0$ Hz, 2H), 7.59 (d, $J = 7.5$ Hz, 2H), 7.26-7.39 (m, 9H), 5.93 (q, $J = 6.5$ Hz, 1H), 5.35 (d, $J = 9.0$ Hz, 1H), 4.35-4.39 (m, 3H), 4.21 (t, $J = 7.0$ Hz, 1H), 2.14-2.20 (m, 1H), 1.56 (d, $J = 6.5$ Hz, 3H), 0.90 (d, $J = 7.0$ Hz, 3H), 0.73 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.5, 156.4, 144.0, 143.9, 141.4, 141.0, 128.6, 128.2, 127.8, 127.1, 126.3, 125.2, 120.0(4), 120.0(3), 73.7, 67.1, 59.0, 47.3, 31.3, 22.1, 19.1, 17.2; HRMS (FTMS-ESI) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{28}\text{H}_{29}\text{NNaO}_4^+$ 466.1989, found 466.1967.



Chiral ester 7e: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-30% (v/v); Colorless oil (38.6 mg, 83% yield, >20:1 dr); ^1H NMR (500 MHz, CDCl_3) δ 7.33-7.37 (m, 4H), 7.28-7.32 (m, 1H), 6.71 (s, 1H), 5.93 (q, $J = 6.5$ Hz, 1H), 4.24-4.26 (m, 1H), 2.41-2.48 (m, 1H), 2.27-2.38 (m, 2H), 2.10-2.17 (m, 1H), 1.56 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.1, 171.3, 140.9, 128.7, 128.2, 126.1, 73.8, 55.6, 29.2, 24.7, 22.1; HRMS (FTMS-ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{16}\text{NO}_3^+$ 234.1125, found 234.1122.

2.5. Synthetic procedure of 5 mmol scale model reaction



N-protected amino acid **1a** (1.56 g, 5.0 mmol, 1.0 equiv.), amino acid ester **2a** (1.08 g, 6.0 mmol, 1.2 equiv.), $\text{Ir}(\text{dF}(\text{CF}_3)\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (56.1 mg, 0.05 mmol, 1 mol %), PPh_3 (1.97 g, 7.5 mmol, 1.5 equiv.) and K_2HPO_4 (1.05 g, 6.0 mmol, 1.2 equiv.) were well mixed in 1,2-dichloroethane (25.0 mL). The resulting mixture was stirred at room

temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). The reaction mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (EtOAc/PE = 20%-40%) to yield dipeptide **3a** in 84% yield (1.98 g, white solid) with >20:1 dr.

2.6. Experimental set-up (Figure S1)

Photochemical reactions were performed with a LED flow reactor WP-TEC-1020HSL (WATTCAS, China). Light flux: Φ (1 m) = 134.53 lm.



Figure S1. The set-up for the reaction

2.7. UV/Vis Absorption Experiments (Figure S2)

UV/Vis absorption spectra of reaction mixtures before, during and after reaction were recorded in 1 cm path quartz cuvettes using a Shimadzu UV-2600 (Figure S2).

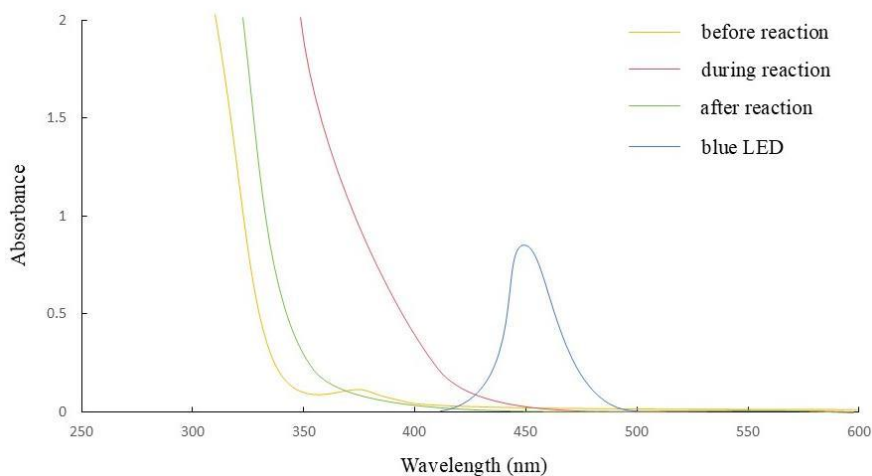
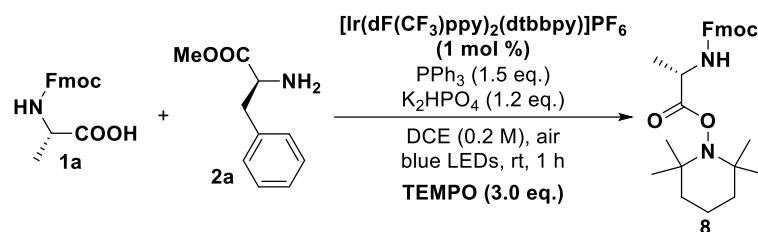
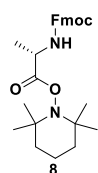


Figure S2. UV/Vis absorption spectrometry of the mixtures

2.8. Mechanistic experiments

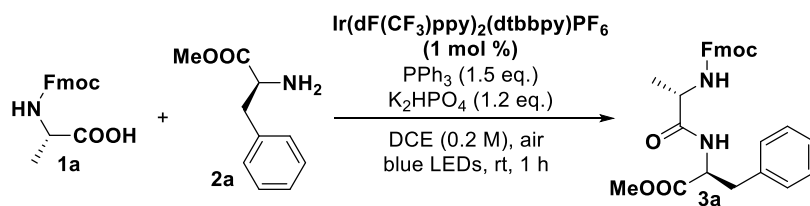


N-protected amino acid **1a** (0.2 mmol, 1.0 equiv.), amino acid ester **2a** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.), K₂HPO₄ (0.24 mmol, 1.2 equiv.) and TEMPO (0.6 mmol, 3.0 equiv.) were well mixed in 1,2-dichloroethane (1.0 mL). The resulting mixture was stirred at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). The reaction mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (EtOAc/PE = 20%-30%) to yield radical-trapping product **8**.



Radical-trapping product 8: Purified by flash chromatography on silica gel, eluting with ethyl acetate/petroleum ether 20%-30% (v/v); Colorless oil (73.7 mg, 82% yield); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.59-7.61 (m, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 5.56 (d, *J* = 6.5 Hz, 1H), 5.52 (d, *J* = 6.5 Hz, 1H), 5.40 (d, *J* = 7.5 Hz, 1H), 4.35-4.45 (m, 3H), 4.22 (t, *J* = 7.0 Hz, 1H), 1.43-1.50 (m, 7H), 1.16 (s, 6H), 1.09 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 172.3, 155.6, 143.9, 143.8, 141.3, 127.7, 127.1, 125.1, 120.0, 95.1, 67.0, 59.9, 59.8, 49.8, 47.2, 39.7, 33.3(0), 33.2(5), 20.2, 18.7, 17.1; HRMS (FTMS-ESI) *m/z*: [M+Na]⁺ calcd for C₂₇H₃₄N₂NaO₄⁺ 473.2411, found 473.2436.

2.9. Experiment supporting catalyst regeneration mechanism



N-protected amino acid **1a** (0.2 mmol, 1.0 equiv.), amino acid ester **2a** (0.24 mmol, 1.2 equiv.), Ir(dF(CF₃)ppy)₂(dtbbpy)PF₆ (1 mol %), PPh₃ (0.3 mmol, 1.5 equiv.) and K₂HPO₄ (0.24 mmol, 1.2 equiv.) were well mixed in 1,2-dichloroethane (1.0 mL). The resulting mixture was stirred at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). Then, N-protected amino acid **1a** (0.2 mmol, 1.0 equiv.), amino acid ester **2a** (0.24 mmol, 1.2 equiv.), PPh₃ (0.3 mmol, 1.5 equiv.), K₂HPO₄ (0.24 mmol,

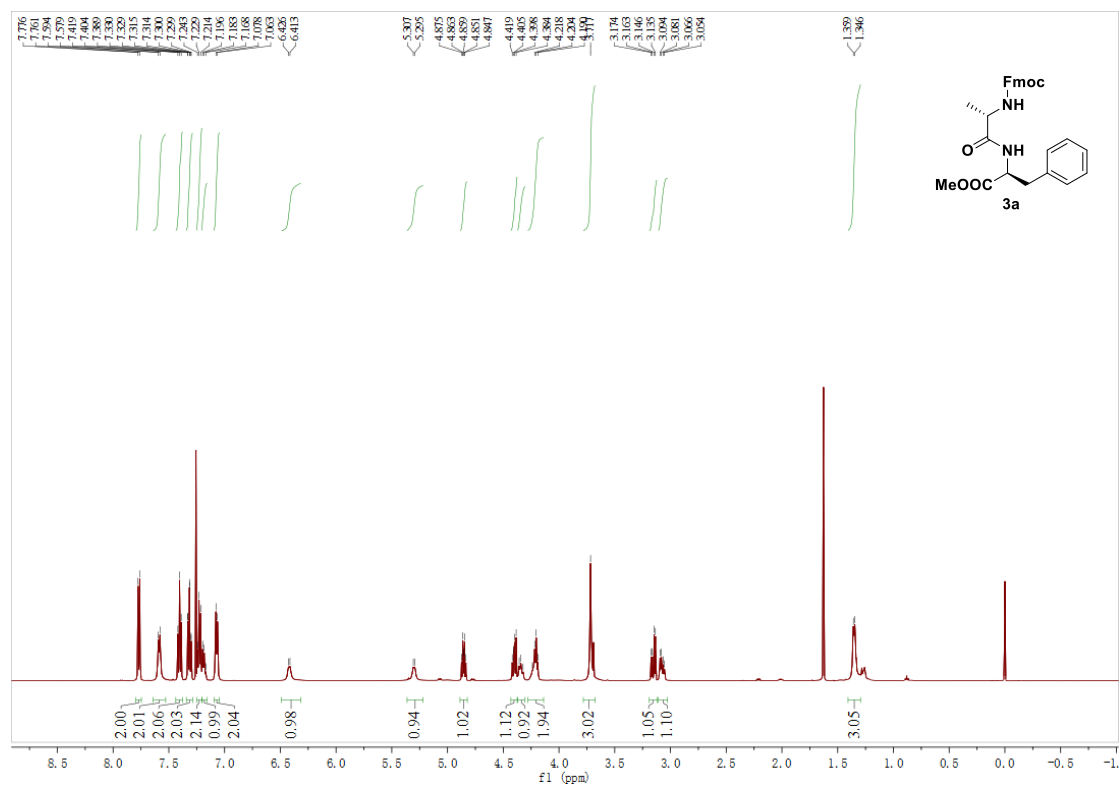
1.2 equiv.) and 1,2-dichloroethane (1.0 mL) were added. The resulting mixture was stirred at room temperature for 1 h under the irradiation of 440 nm blue LEDs (10 W). The reaction mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (EtOAc/PE = 20%-30%) to yield dipeptide **3a** in 88% yield (166.7 mg, white solid) with >20:1 dr.

References

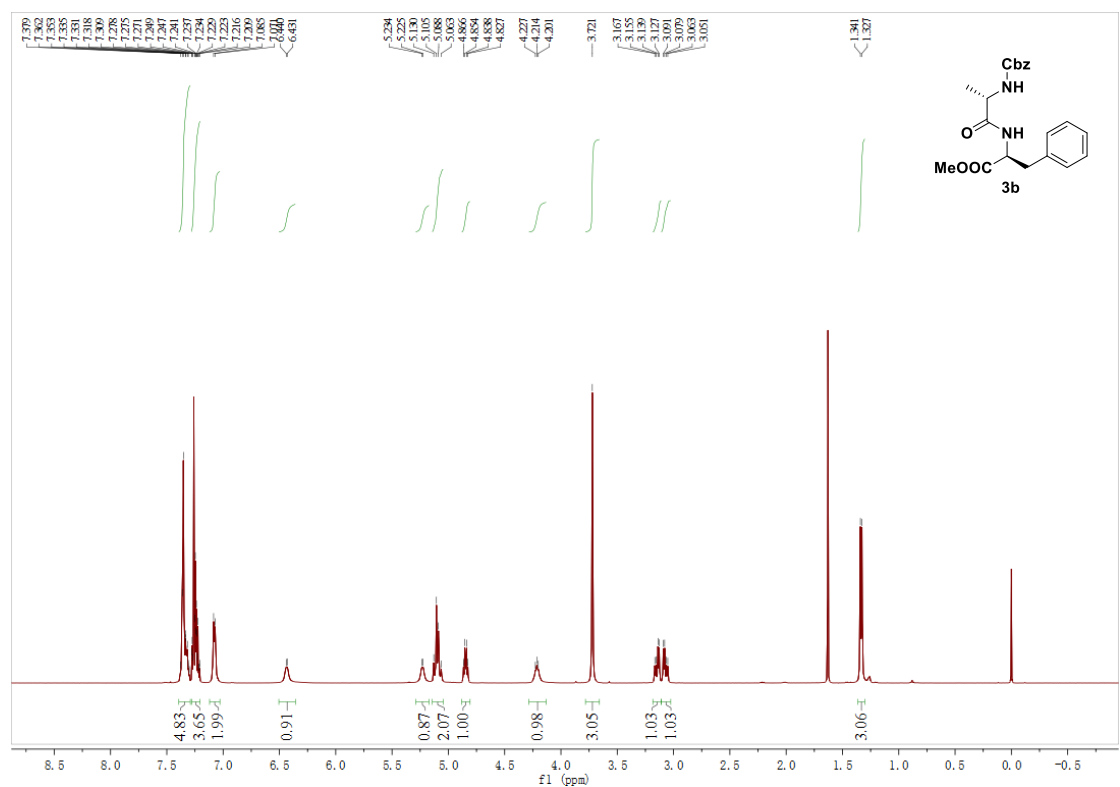
- (1) S. Sharma, N. W. Buchbinder, W. M. Braje, S. Handa, Fast Amide Couplings in Water: Extraction, Column Chromatography, and Crystallization not Required. *Org. Lett.*, 2020, **22**, 5737-5740.
- (2) H. Li, X. Jiang, Y. Ye, C. Fan, T. Romoff, M. Goodman, 3-(Diethoxyphosphoryloxy)-1,2,3-Benzotriazin-4(3H)-One (DEPBT): A New Coupling Reagent with Remarkable Resistance to Racemization. *Org. Lett.*, 1999, **1**, 91-93.
- (3) E. Suárez-Picado, E. Quiñoá, R. Riguera, F. Freire, Chiral Overpass Induction in Dynamic Helical Polymers Bearing Pendant Groups with Two Chiral Centers. *Angew. Chem., Int. Ed.*, 2020, **59**, 4537-4543.
- (4) L. Hu, S. Xu, Z. Zhao, Y. Yang, Z. Peng, M. Yang, C. Wang, J. Zhao, Ynamides as Racemization-Free Coupling Reagents for Amide and Peptide Synthesis. *J. Am. Chem. Soc.*, 2016, **138**, 13135-13138.
- (5) J.-W. Ren, M.-N. Tong, Y.-F. Zhao, F. Ni, Synthesis of Dipeptide, Amide, and Ester without Racemization by Oxalyl Chloride and Catalytic Triphenylphosphine Oxide. *Org. Lett.*, 2021, **23**, 7497-7502.

3. NMR Spectra

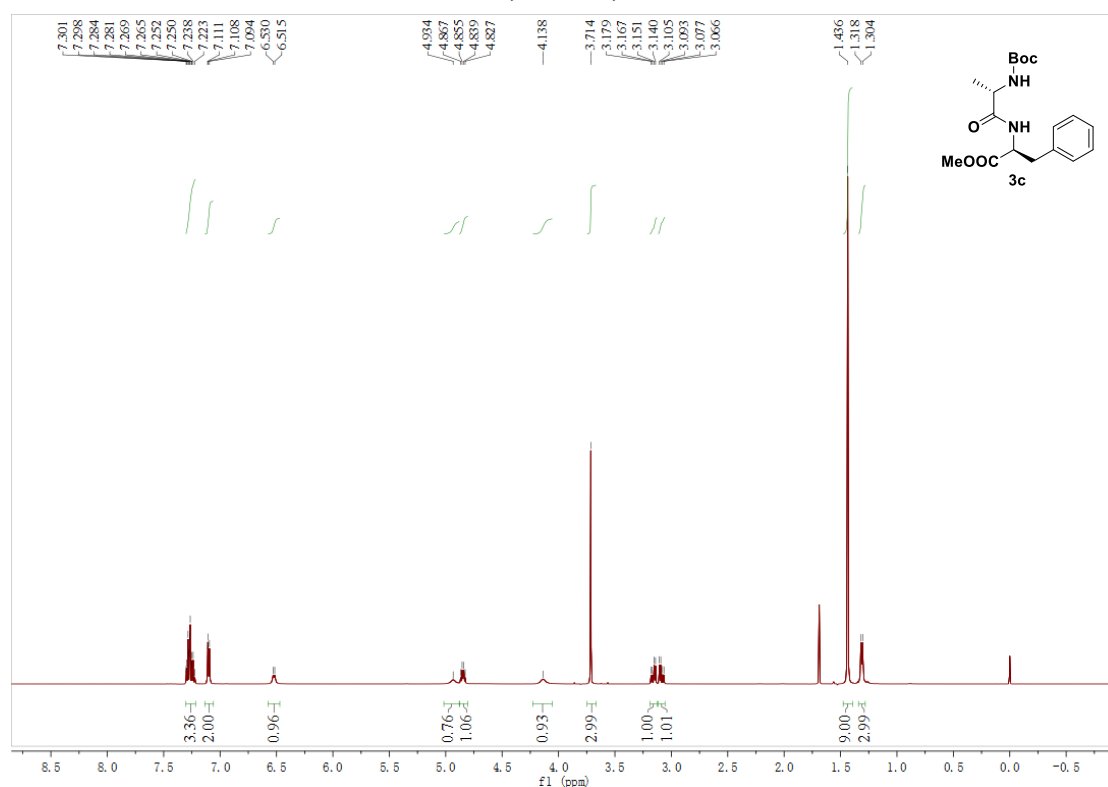
500 MHz, CDCl₃, ¹H NMR



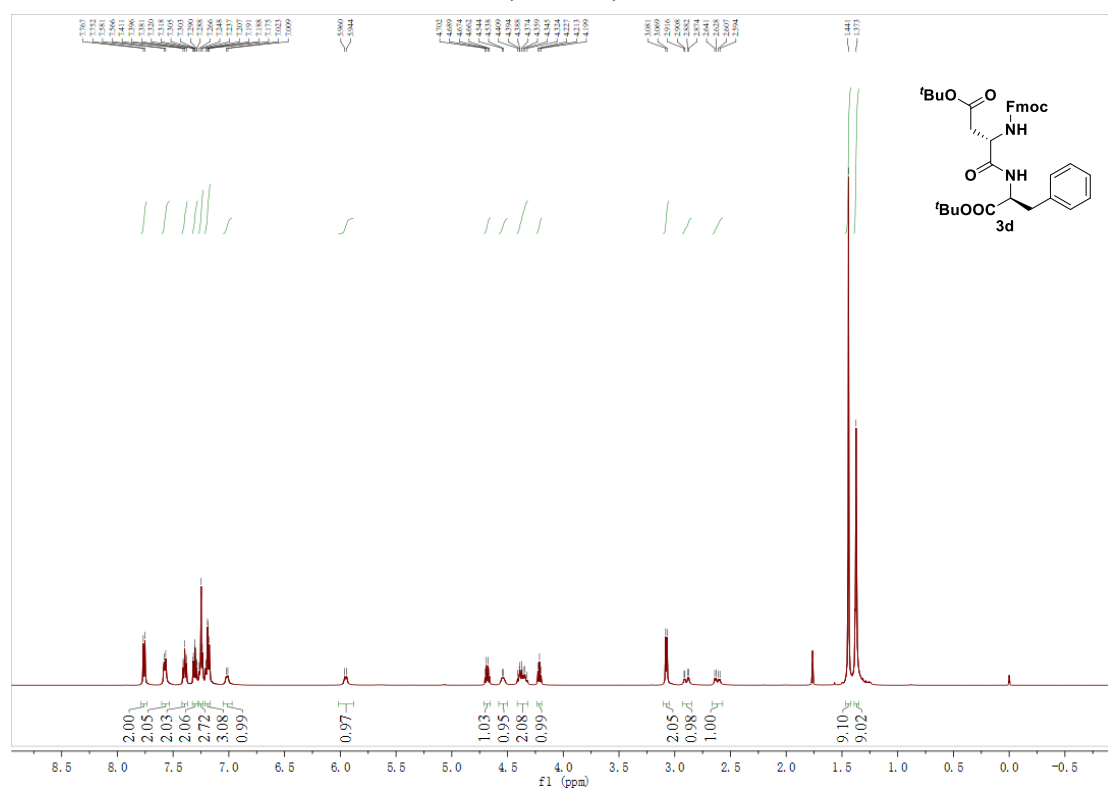
500 MHz, CDCl₃, ¹H NMR



500 MHz, CDCl₃, ¹H NMR



500 MHz, CDCl₃, ¹H NMR



Chemical structure of **3e** is shown in the top right corner. The structure is a derivative of a chiral amine, featuring a phenyl group (Ph), a tert-butyl ester group (tBuOOC), and an isopropyl group, with a chiral center marked with a wedge bond.

The ^1H NMR spectrum (CDCl₃) shows the following peaks (ppm) and integrations:

- 7.73, 7.78, 7.57, 7.54, 7.50, 7.07, 7.40, 7.38, 7.34, 7.28, 7.26, 7.24, 7.22, 7.20, 7.18, 7.16, 7.14, 7.12, 7.10, 7.08, 7.06, 7.04, 7.02, 7.00, 6.98, 6.96, 6.94, 6.92, 6.90, 6.88, 6.86, 6.84, 6.82, 6.80, 6.78, 6.76, 6.74, 6.72, 6.70, 6.68, 6.66, 6.64, 6.62, 6.60, 6.58, 6.56, 6.54, 6.52, 6.50, 6.48, 6.46, 6.44, 6.42, 6.40, 6.38, 6.36, 6.34, 6.32, 6.30, 6.28, 6.26, 6.24, 6.22, 6.20, 6.18, 6.16, 6.14, 6.12, 6.10, 6.08, 6.06, 6.04, 6.02, 6.00, 5.98, 5.96, 5.94, 5.92, 5.90, 5.88, 5.86, 5.84, 5.82, 5.80, 5.78, 5.76, 5.74, 5.72, 5.70, 5.68, 5.66, 5.64, 5.62, 5.60, 5.58, 5.56, 5.54, 5.52, 5.50, 5.48, 5.46, 5.44, 5.42, 5.40, 5.38, 5.36, 5.34, 5.32, 5.30, 5.28, 5.26, 5.24, 5.22, 5.20, 5.18, 5.16, 5.14, 5.12, 5.10, 5.08, 5.06, 5.04, 5.02, 5.00, 4.98, 4.96, 4.94, 4.92, 4.90, 4.88, 4.86, 4.84, 4.82, 4.80, 4.78, 4.76, 4.74, 4.72, 4.70, 4.68, 4.66, 4.64, 4.62, 4.60, 4.58, 4.56, 4.54, 4.52, 4.50, 4.48, 4.46, 4.44, 4.42, 4.40, 4.38, 4.36, 4.34, 4.32, 4.30, 4.28, 4.26, 4.24, 4.22, 4.20, 4.18, 4.16, 4.14, 4.12, 4.10, 4.08, 4.06, 4.04, 4.02, 4.00, 3.98, 3.96, 3.94, 3.92, 3.90, 3.88, 3.86, 3.84, 3.82, 3.80, 3.78, 3.76, 3.74, 3.72, 3.70, 3.68, 3.66, 3.64, 3.62, 3.60, 3.58, 3.56, 3.54, 3.52, 3.50, 3.48, 3.46, 3.44, 3.42, 3.40, 3.38, 3.36, 3.34, 3.32, 3.30, 3.28, 3.26, 3.24, 3.22, 3.20, 3.18, 3.16, 3.14, 3.12, 3.10, 3.08, 3.06, 3.04, 3.02, 3.00, 2.98, 2.96, 2.94, 2.92, 2.90, 2.88, 2.86, 2.84, 2.82, 2.80, 2.78, 2.76, 2.74, 2.72, 2.70, 2.68, 2.66, 2.64, 2.62, 2.60, 2.58, 2.56, 2.54, 2.52, 2.50, 2.48, 2.46, 2.44, 2.42, 2.40, 2.38, 2.36, 2.34, 2.32, 2.30, 2.28, 2.26, 2.24, 2.22, 2.20, 2.18, 2.16, 2.14, 2.12, 2.10, 2.08, 2.06, 2.04, 2.02, 2.00, 1.98, 1.96, 1.94, 1.92, 1.90, 1.88, 1.86, 1.84, 1.82, 1.80, 1.78, 1.76, 1.74, 1.72, 1.70, 1.68, 1.66, 1.64, 1.62, 1.60, 1.58, 1.56, 1.54, 1.52, 1.50, 1.48, 1.46, 1.44, 1.42, 1.40, 1.38, 1.36, 1.34, 1.32, 1.30, 1.28, 1.26, 1.24, 1.22, 1.20, 1.18, 1.16, 1.14, 1.12, 1.10, 1.08, 1.06, 1.04, 1.02, 1.00, 0.98, 0.96, 0.94, 0.92, 0.90, 0.88, 0.86, 0.84, 0.82, 0.80, 0.78, 0.76, 0.74, 0.72, 0.70, 0.68, 0.66, 0.64, 0.62, 0.60, 0.58, 0.56, 0.54, 0.52, 0.50, 0.48, 0.46, 0.44, 0.42, 0.40, 0.38, 0.36, 0.34, 0.32, 0.30, 0.28, 0.26, 0.24, 0.22, 0.20, 0.18, 0.16, 0.14, 0.12, 0.10, 0.08, 0.06, 0.04, 0.02, 0.00, -0.02, -0.04, -0.06, -0.08, -0.10, -0.12, -0.14, -0.16, -0.18, -0.20, -0.22, -0.24, -0.26, -0.28, -0.30, -0.32, -0.34, -0.36, -0.38, -0.40, -0.42, -0.44, -0.46, -0.48, -0.50, -0.52, -0.54, -0.56, -0.58, -0.60, -0.62, -0.64, -0.66, -0.68, -0.70, -0.72, -0.74, -0.76, -0.78, -0.80, -0.82, -0.84, -0.86, -0.88, -0.90, -0.92, -0.94, -0.96, -0.98, -1.00, -1.02, -1.04, -1.06, -1.08, -1.10, -1.12, -1.14, -1.16, -1.18, -1.20, -1.22, -1.24, -1.26, -1.28, -1.30, -1.32, -1.34, -1.36, -1.38, -1.40, -1.42, -1.44, -1.46, -1.48, -1.50, -1.52, -1.54, -1.56, -1.58, -1.60, -1.62, -1.64, -1.66, -1.68, -1.70, -1.72, -1.74, -1.76, -1.78, -1.80, -1.82, -1.84, -1.86, -1.88, -1.90, -1.92, -1.94, -1.96, -1.98, -2.00, -2.02, -2.04, -2.06, -2.08, -2.10, -2.12, -2.14, -2.16, -2.18, -2.20, -2.22, -2.24, -2.26, -2.28, -2.30, -2.32, -2.34, -2.36, -2.38, -2.40, -2.42, -2.44, -2.46, -2.48, -2.50, -2.52, -2.54, -2.56, -2.58, -2.60, -2.62, -2.64, -2.66, -2.68, -2.70, -2.72, -2.74, -2.76, -2.78, -2.80, -2.82, -2.84, -2.86, -2.88, -2.90, -2.92, -2.94, -2.96, -2.98, -3.00, -3.02, -3.04, -3.06, -3.08, -3.10, -3.12, -3.14, -3.16, -3.18, -3.20, -3.22, -3.24, -3.26, -3.28, -3.30, -3.32, -3.34, -3.36, -3.38, -3.40, -3.42, -3.44, -3.46, -3.48, -3.50, -3.52, -3.54, -3.56, -3.58, -3.60, -3.62, -3.64, -3.66, -3.68, -3.70, -3.72, -3.74, -3.76, -3.78, -3.80, -3.82, -3.84, -3.86, -3.88, -3.90, -3.92, -3.94, -3.96, -3.98, -4.00, -4.02, -4.04, -4.06, -4.08, -4.10, -4.12, -4.14, -4.16, -4.18, -4.20, -4.22, -4.24, -4.26, -4.28, -4.30, -4.32, -4.34, -4.36, -4.38, -4.40, -4.42, -4.44, -4.46, -4.48, -4.50, -4.52, -4.54, -4.56, -4.58, -4.60, -4.62, -4.64, -4.66, -4.68, -4.70, -4.72, -4.74, -4.76, -4.78, -4.80, -4.82, -4.84, -4.86, -4.88, -4.90, -4.92, -4.94, -4.96, -4.98, -5.00, -5.02, -5.04, -5.06, -5.08, -5.10, -5.12, -5.14, -5.16, -5.18, -5.20, -5.22, -5.24, -5.26, -5.28,

Chemical structure of 3f:

CC(C)C[C@@H](C(=O)OCC)C(=O)N[C@@H](C(=O)OCC)C(F)(F)F

¹H NMR spectrum (CDCl₃):

Chemical Shift (ppm)	Integration
~7.2	0.77
~5.7	0.87
~4.2	1.02
~3.6	2.06
~3.3	2.05
~1.5	1.01
~1.2	0.97
~1.5	0.86
~1.5	0.94
~1.5	1.07
~1.2	8.84
~1.2	9.06
~0.9	6.00

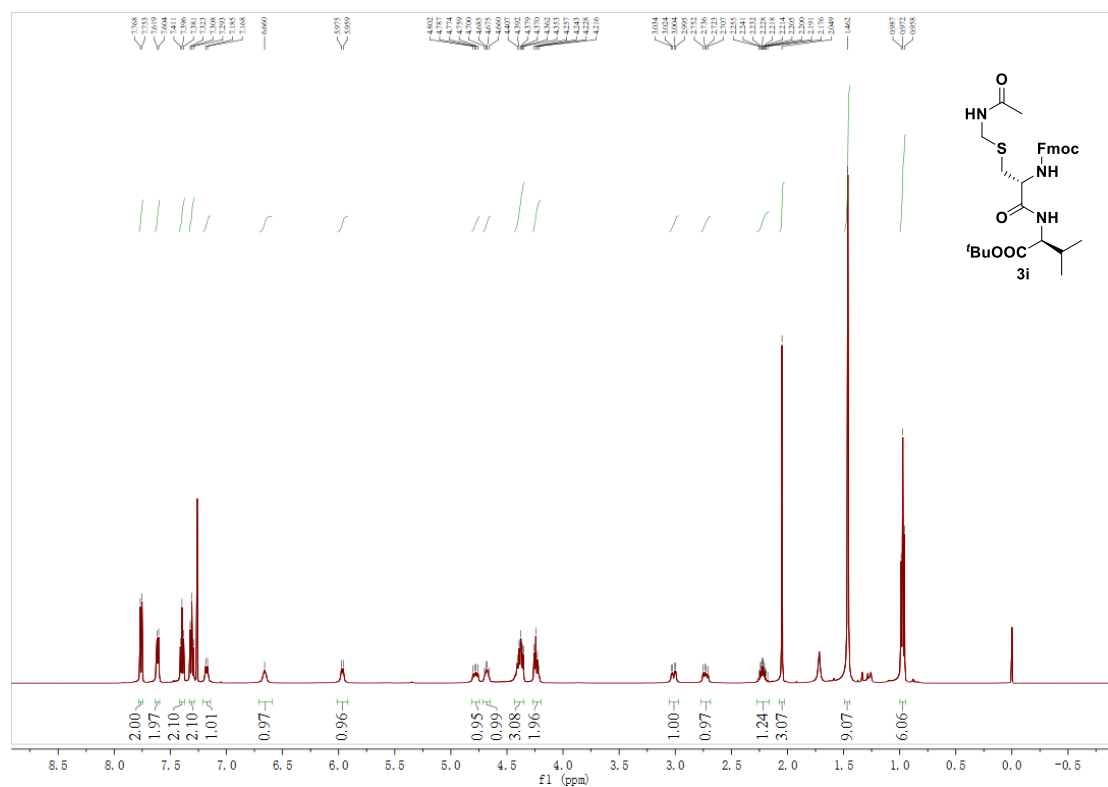
Chemical structure of 3g: CC(C)[C@H](NC(=O)OC(C)(C)C)C(=O)N[C@@H](C(C)C)C1=CC=C(C=C1)C2=CC=CC=C2

¹H NMR spectrum (CDCl₃):

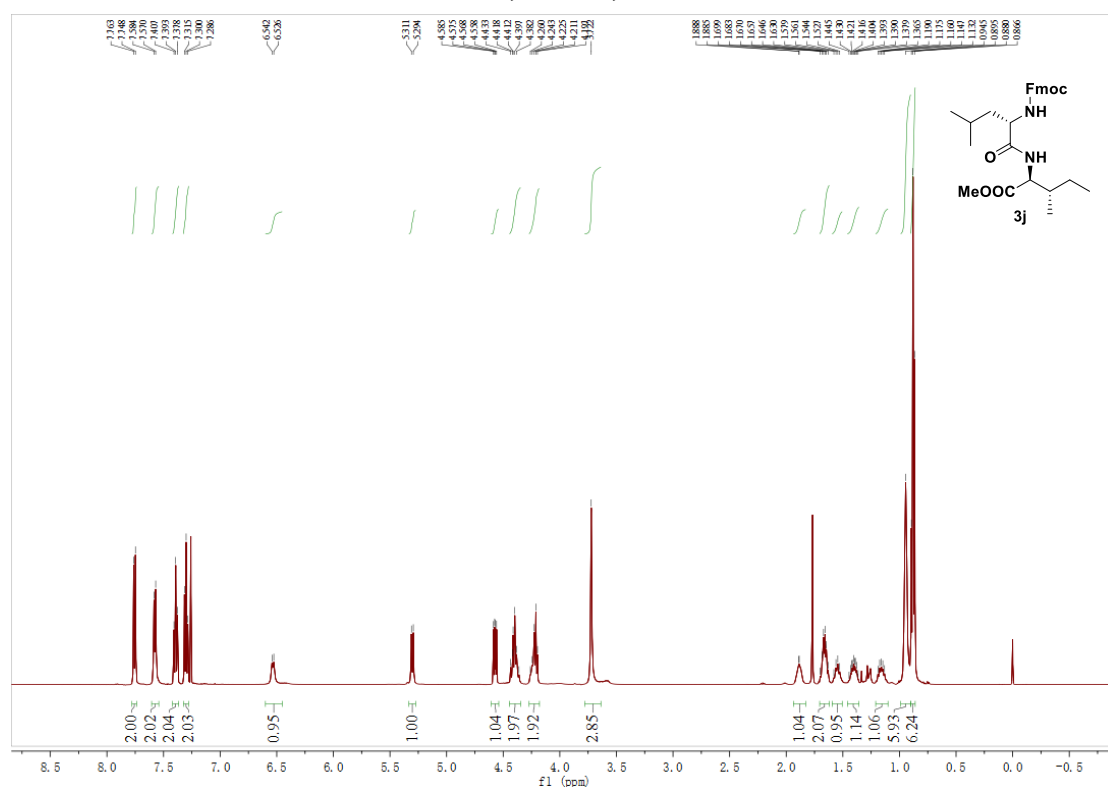
- Chemical shift (ppm):** 7.567, 7.565, 7.563, 7.560, 7.558, 7.541, 7.536, 7.534, 7.531, 7.528, 7.526, 7.509, 7.507, 7.305, 7.255, 7.252, 7.250, 6.285, 6.280, 5.526, 5.520, 4.469, 4.488, 4.482, 4.481, 4.480, 4.465, 4.454, 4.428, 4.407, 4.406, 4.384, 4.353, 4.225, 4.213, 4.213, 4.159, 1.070, 1.060, 1.053, 1.052, 1.051, 1.050, 1.038, 1.382, 1.380, 1.379, 1.378, 1.340, 1.334, 1.334, 1.328, 1.188, 0.992, 0.986, 0.981, 0.971, 0.969, 0.899.
- Integration values:** 2.00, 2.02, 2.03, 2.02, 0.89, 0.87, 1.11, 1.89, 1.88, 5.98, 9.08, 5.77, 6.15.

Chemical structure of **3h** is shown in the top right corner. The structure is a dipeptide derivative: CC(C)[C@H](NC(=O)[C@@H](C(C)C)C(=O)Nc1ccc2ccccc12)c3ccccc3. The structure shows a chiral center with a benzyl group (Fmoc) and a tert-butyl ester group.

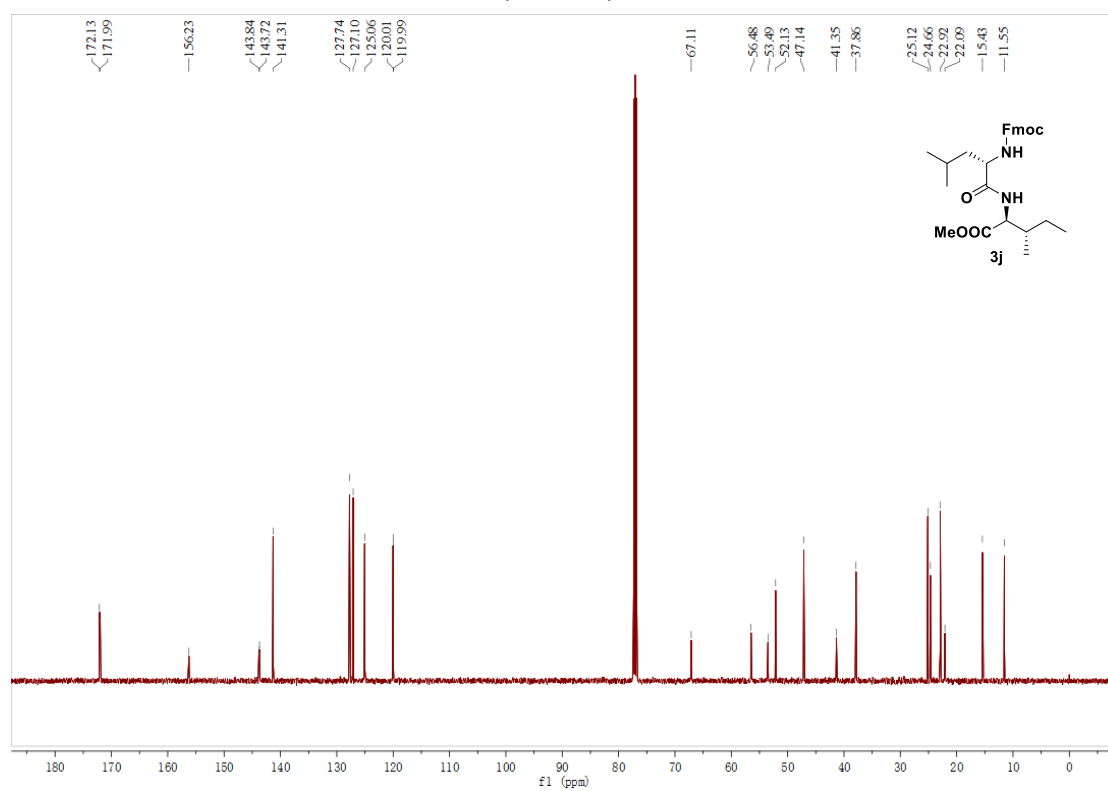
500 MHz, CDCl₃, ¹H NMR



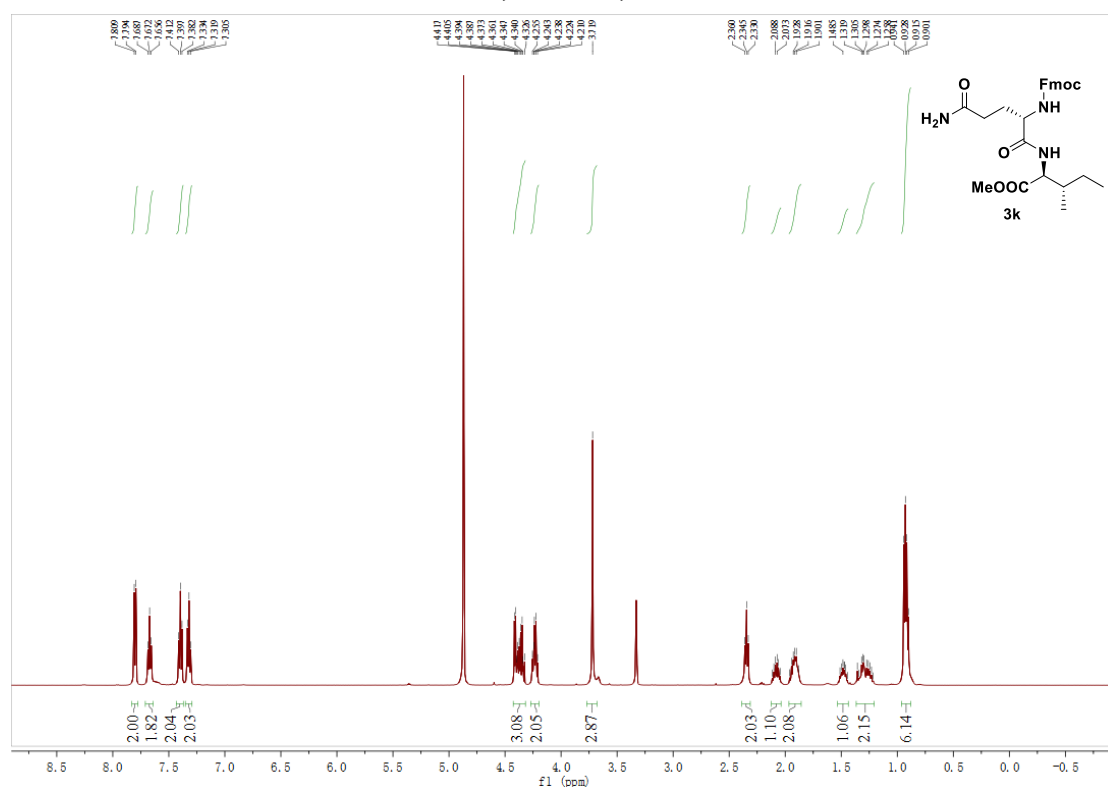
500 MHz, CDCl₃, ¹H NMR



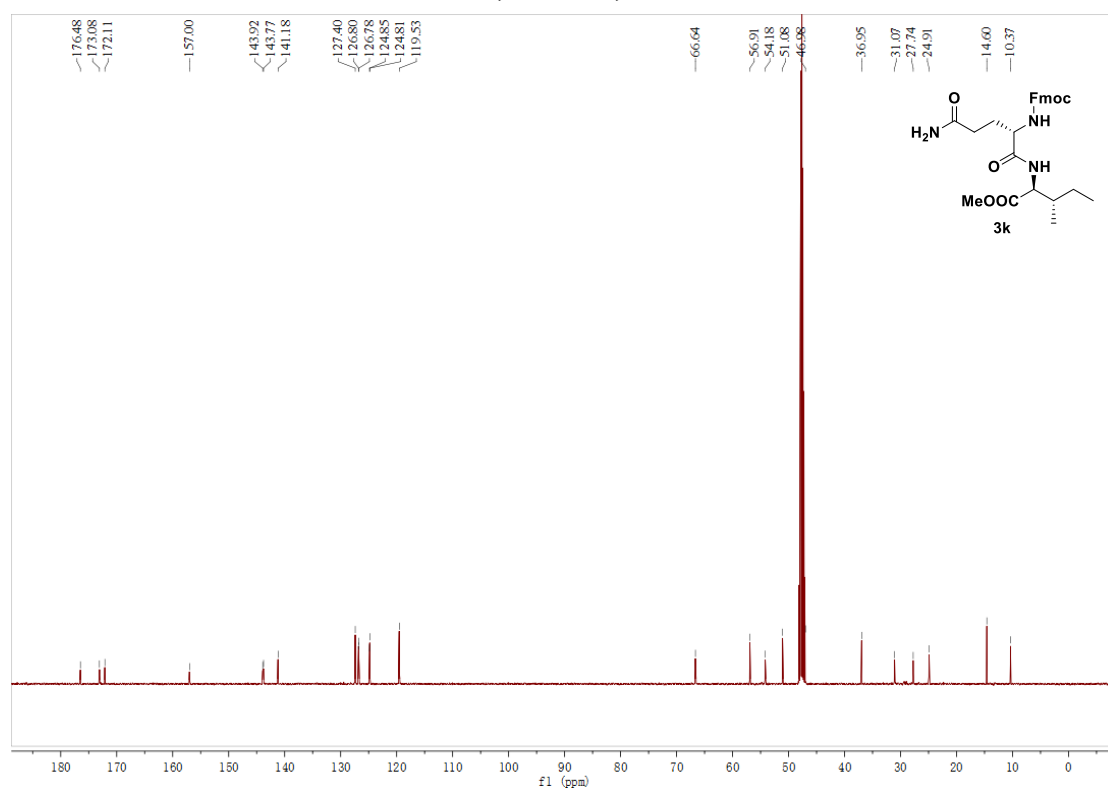
125 MHz, CDCl₃, ¹³C NMR



500 MHz, CD₃OD, ¹H NMR



125 MHz, CD₃OD, ¹³C NMR



Chemical structure of 3l: CCOC(=O)C[C@H](NC(=O)C[C@@H](N)C(=O)OCC(F)(F)F)C(=O)OCC(F)(F)F

¹H NMR spectrum (CDCl₃):

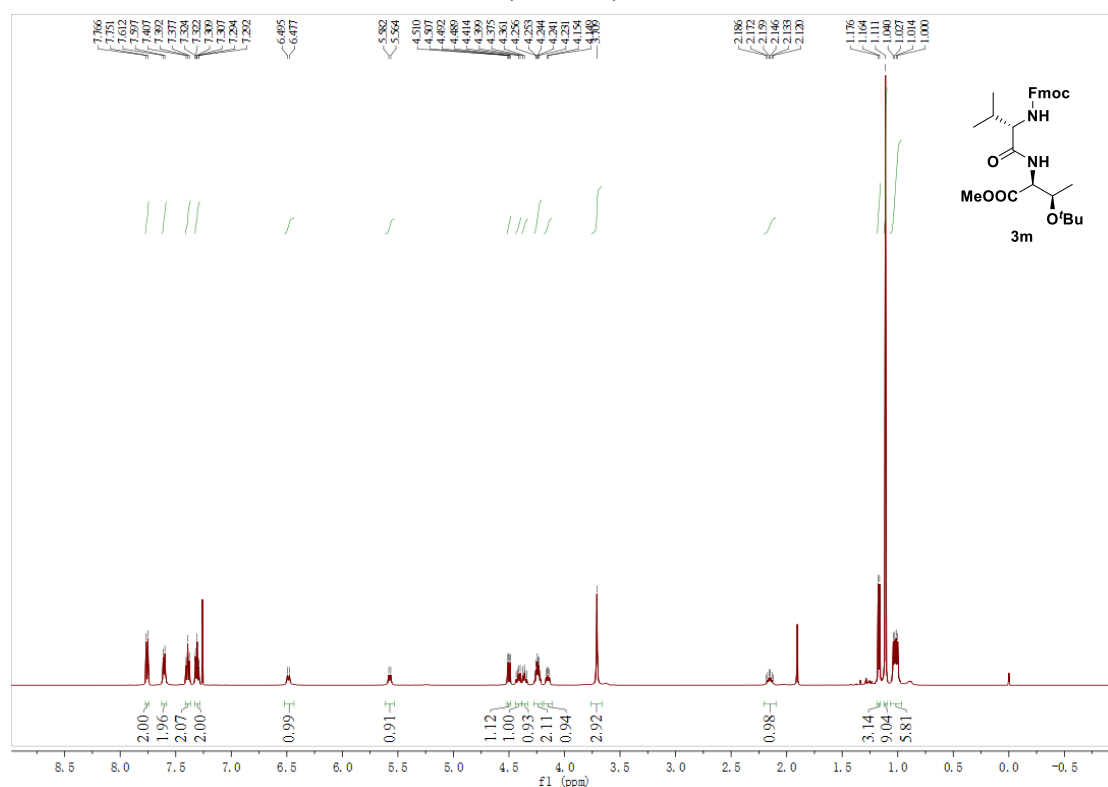
Chemical Shift (ppm)	Integration
7.25, 7.20, 7.15, 7.10, 7.05	2.00, 1.98, 2.03, 2.02, 0.90
6.00	0.89
4.35, 4.25, 4.15	1.94, 2.07, 1.00
3.55, 3.50	3.00, 2.96
2.95	1.01
2.45, 2.35, 2.25, 2.15, 2.05	0.98, 2.11, 1.05, 1.05
1.55, 1.50, 1.45	9.22

Chemical structure of compound **31** is shown in the top right corner. The structure is a dipeptide derivative: CCOC(=O)C[C@H](NC(=O)[C@@H](NC(=O)OC(C)(C)C)C(=O)OC(C)(C)C)C(=O)OC(C)(C)C. The structure includes a methyl ester group (MeOOC), a chiral center (CH), an amide group (NH), and a tert-butyl ester group (tBuOOC).

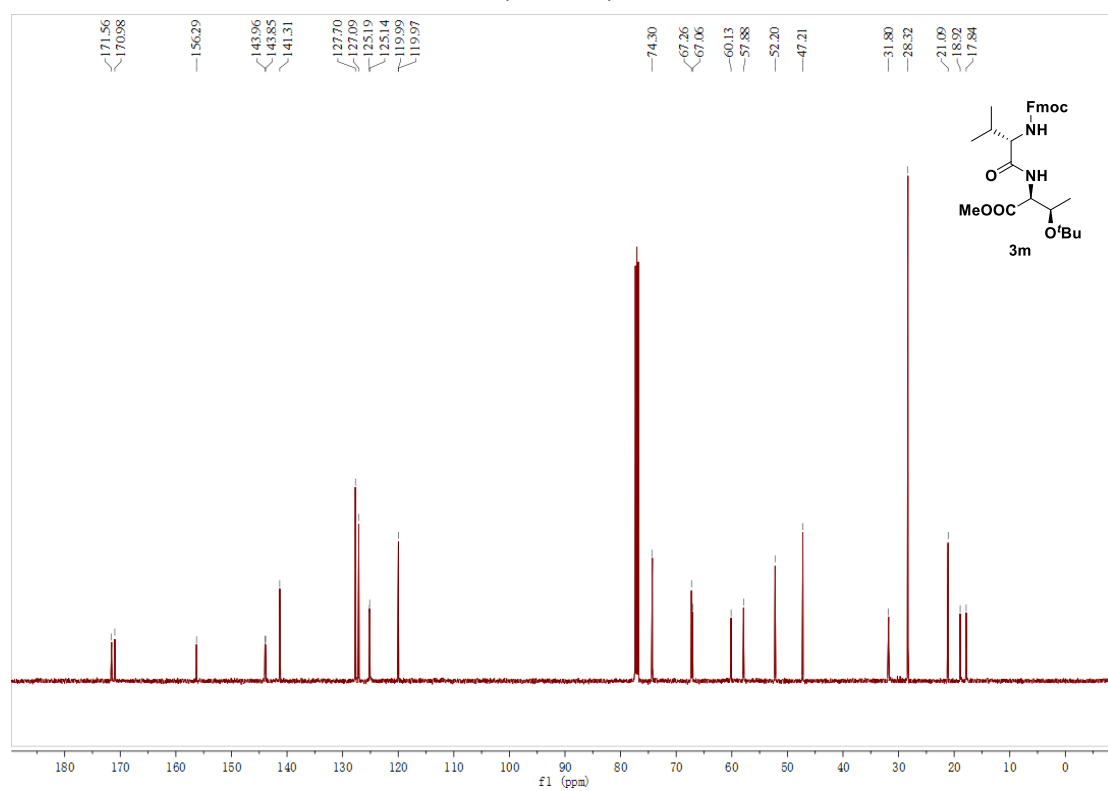
The ^{13}C NMR spectrum (CDCl₃) shows the following chemical shifts (ppm):

- 173.24, 171.75, 171.42, 170.61 (amide carbonyls)
- 156.03 (Fmoc carbonyl)
- 143.84, 143.66, 141.32 (aromatic)
- 127.78, 127.12, 125.10, 120.04 (aromatic)
- 82.03 (CDCl₃ solvent triplet)
- 67.33 (CH-OH)
- 52.55, 51.89, 51.80, 51.05, 47.14 (ester and amide)
- 37.45 (CH₂)
- 29.85, 28.03, 27.15 (methyls)

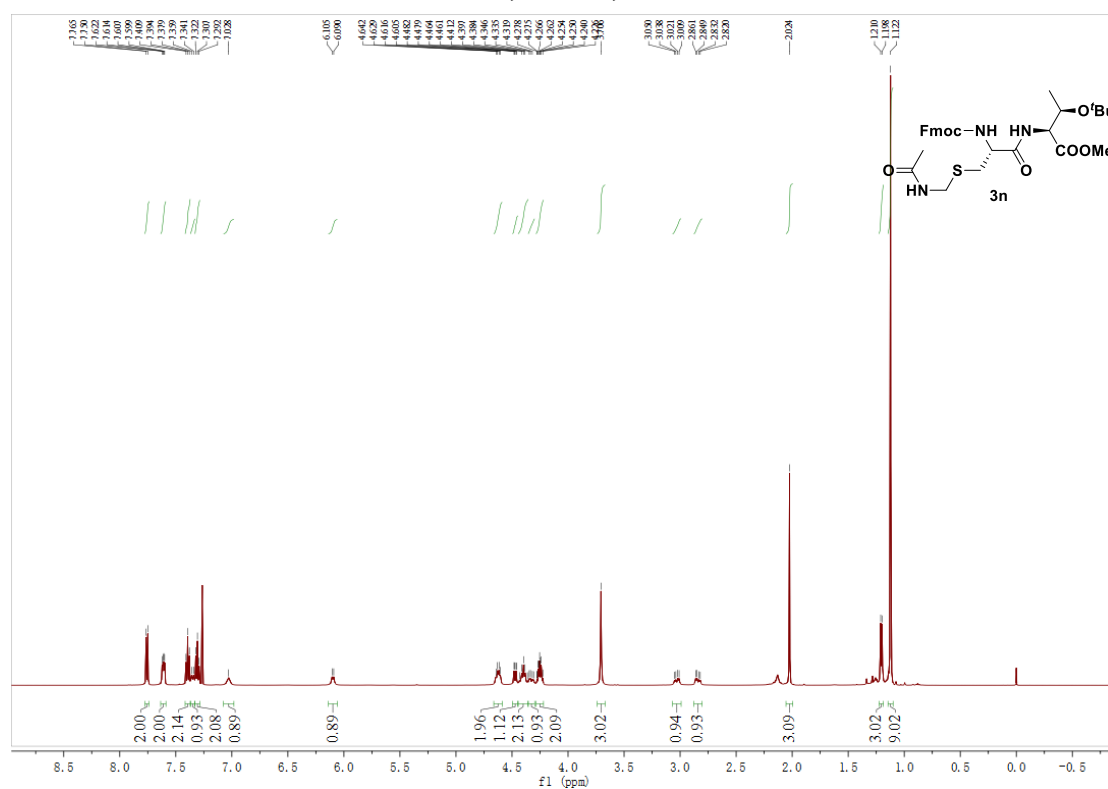
500 MHz, CDCl₃, ¹H NMR



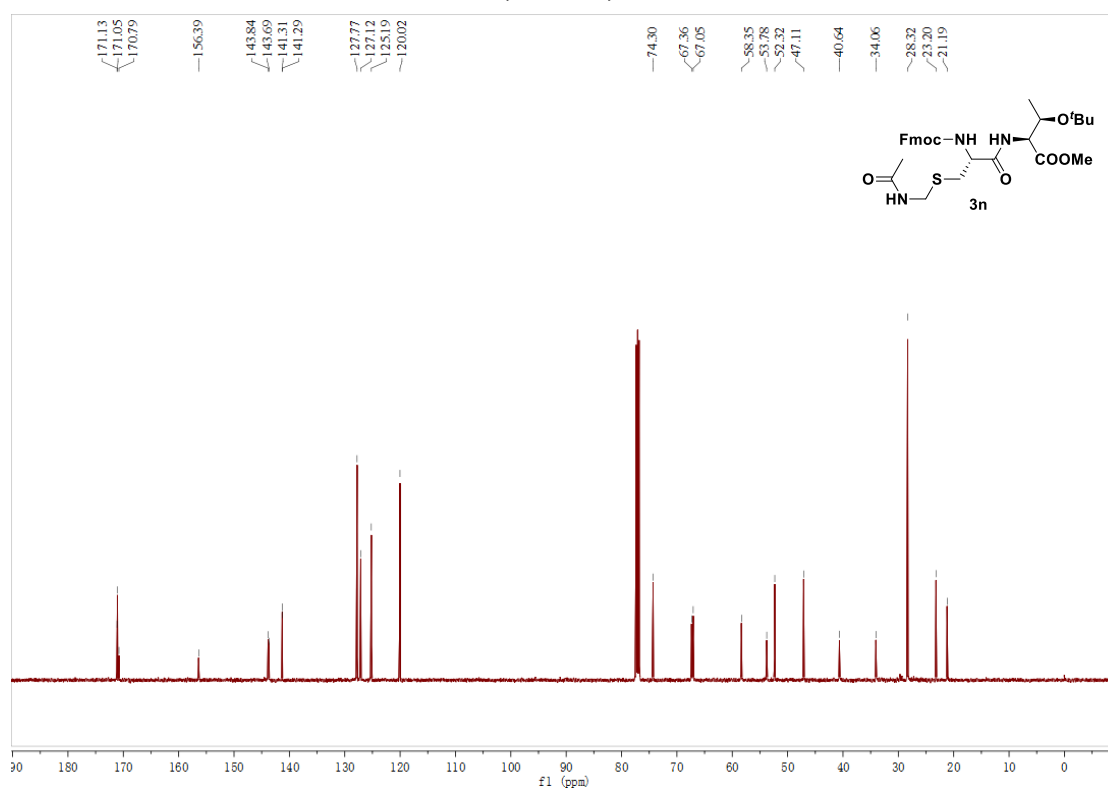
125 MHz, CDCl₃, ¹³C NMR



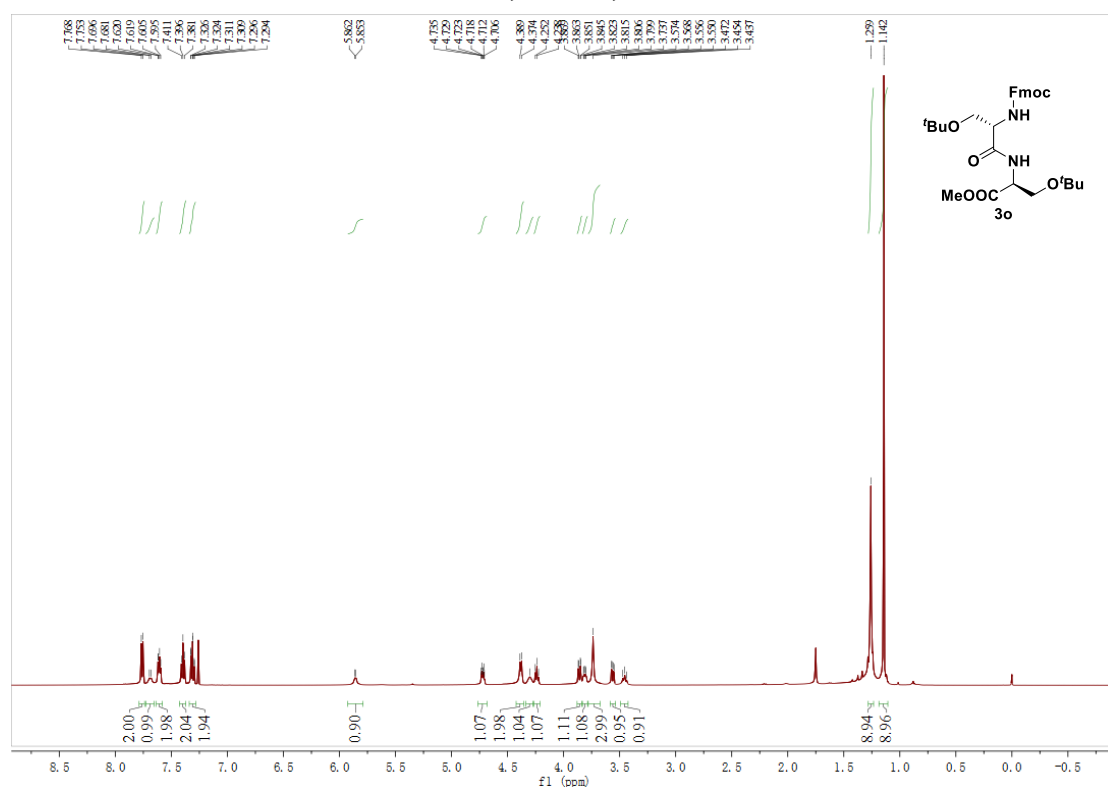
500 MHz, CDCl₃, ¹H NMR



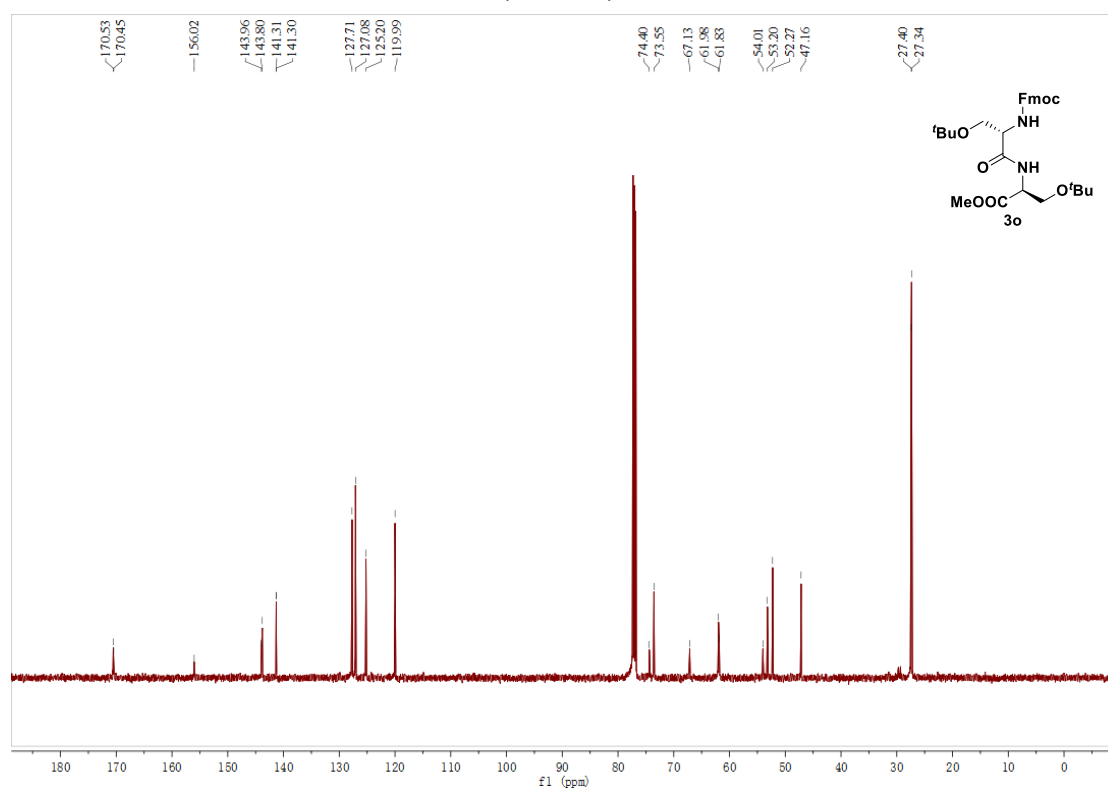
125 MHz, CDCl₃, ¹³C NMR



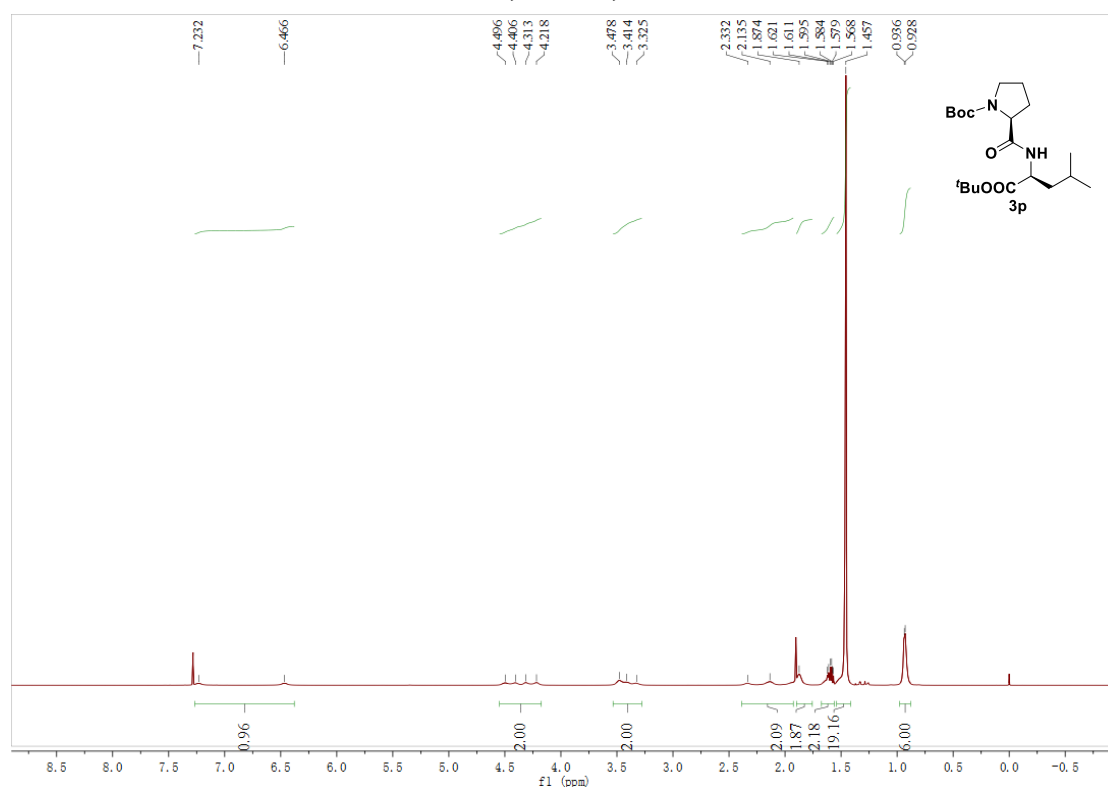
500 MHz, CDCl₃, ¹H NMR



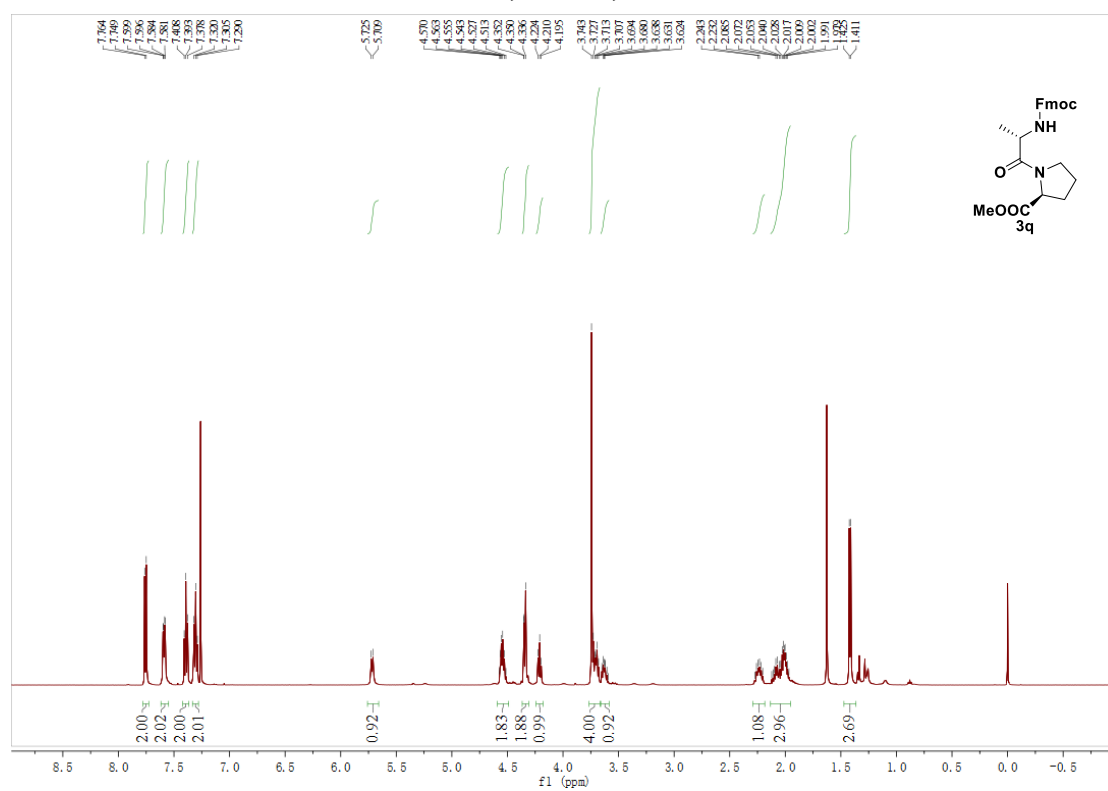
125 MHz, CDCl₃, ¹³C NMR



500 MHz, CDCl₃, ¹H NMR



500 MHz, CDCl₃, ¹H NMR



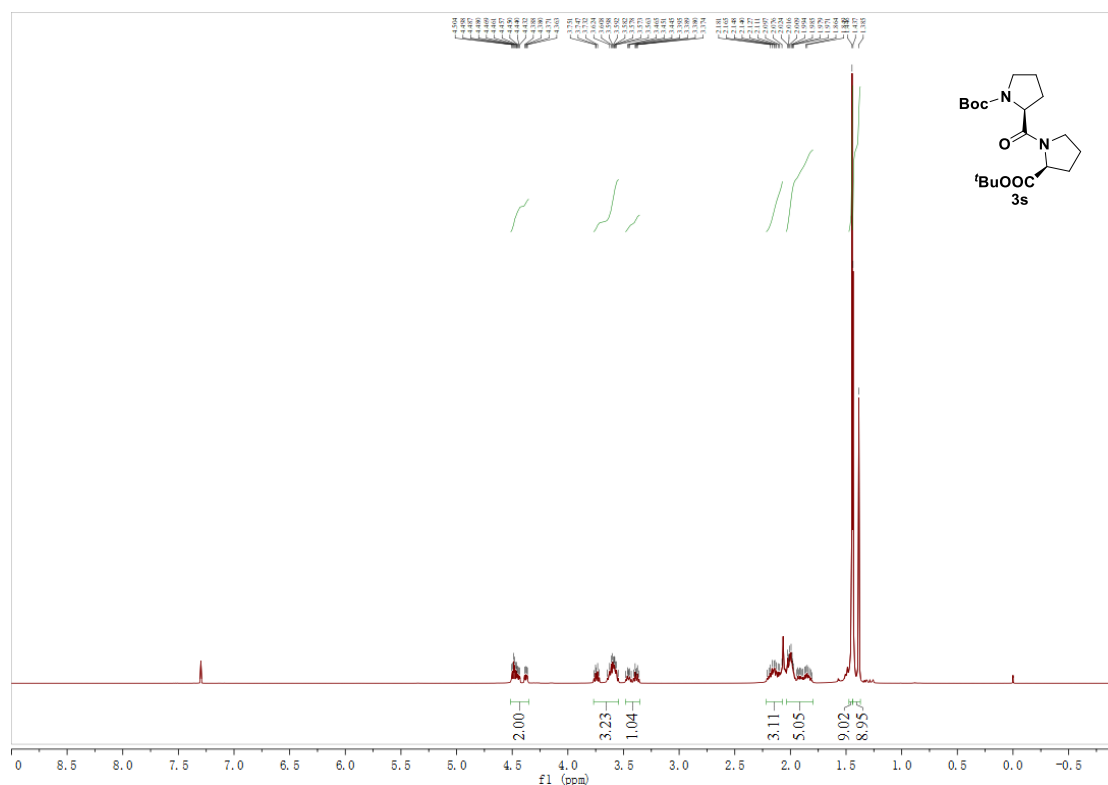
Chemical structure of **3r** is shown in the top right corner. The structure is a pyrrolidine ring substituted with a tert-butyl ester group ($t\text{BuOOC}$), an Fmoc group (Fmoc-NH), and a 2-amino-3-methylbutyl side chain ($\text{H}_2\text{N-CH}_2\text{-CH(CH}_3\text{)-CH}_2\text{-}$).

Chemical structure of **3r** is shown, which is a substituted pyrrolidine derivative. The structure includes an Fmoc group, a tert-butyl ester group, and a side chain with an amide and an amine group.

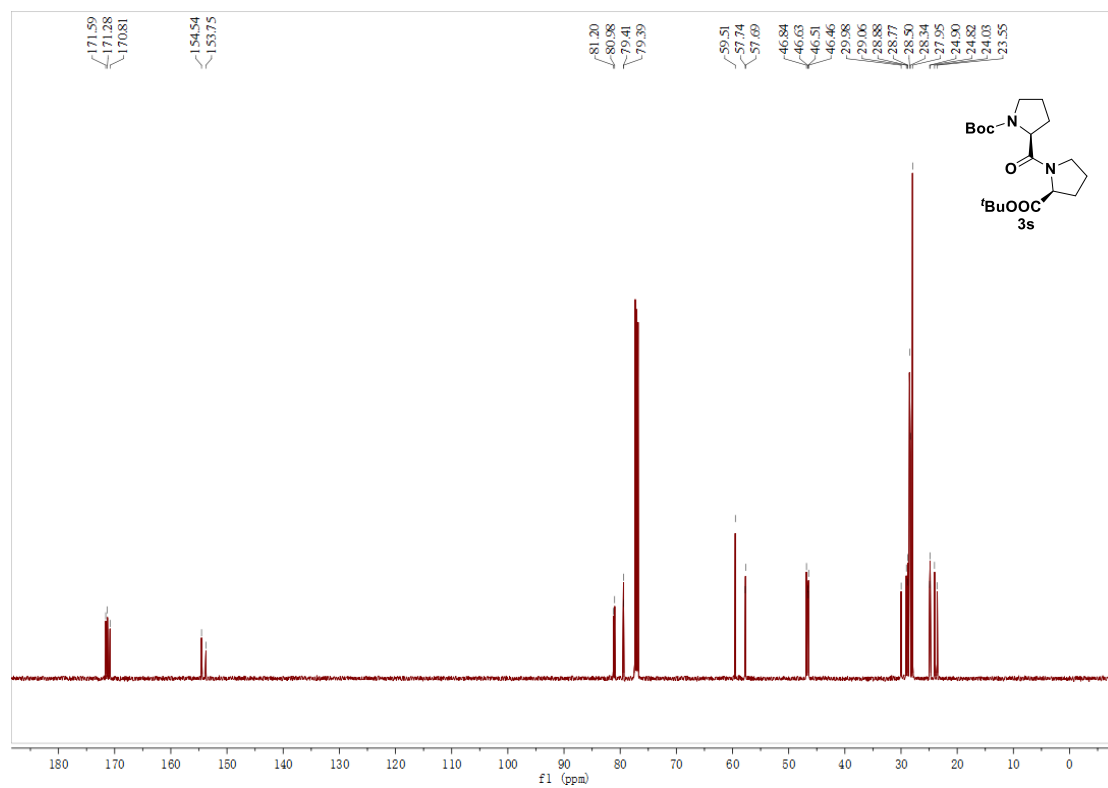
¹³C NMR spectrum (CDCl₃) of **3r** is displayed below the structure. The spectrum shows peaks corresponding to the chemical shifts of the carbon atoms in the molecule, with the following values (ppm):

- 176.25
- 171.49
- 171.43
- 157.13
- 143.88
- 143.79
- 141.19
- 127.40
- 126.59
- 124.85
- 124.83
- 119.54
- 81.36
- 66.61
- 59.96
- 51.97
- 47.00
- 46.53
- 30.57
- 28.68
- 26.89
- 26.84
- 24.41

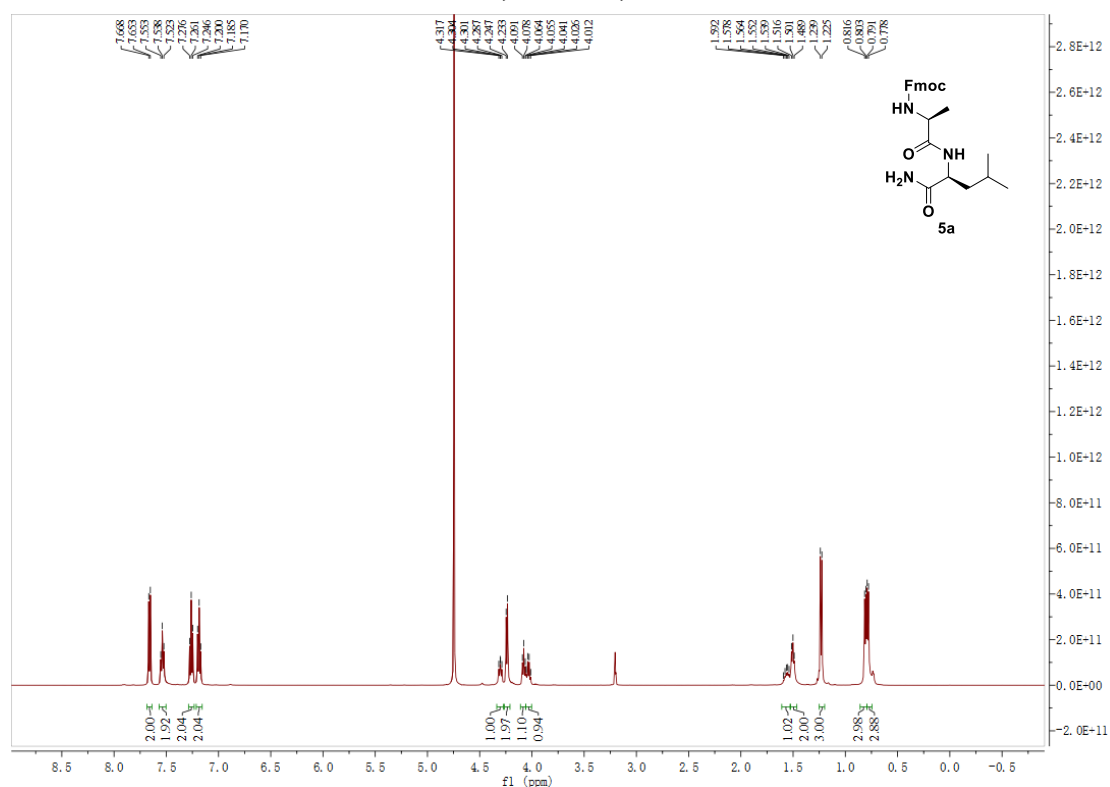
500 MHz, CDCl₃, ¹H NMR



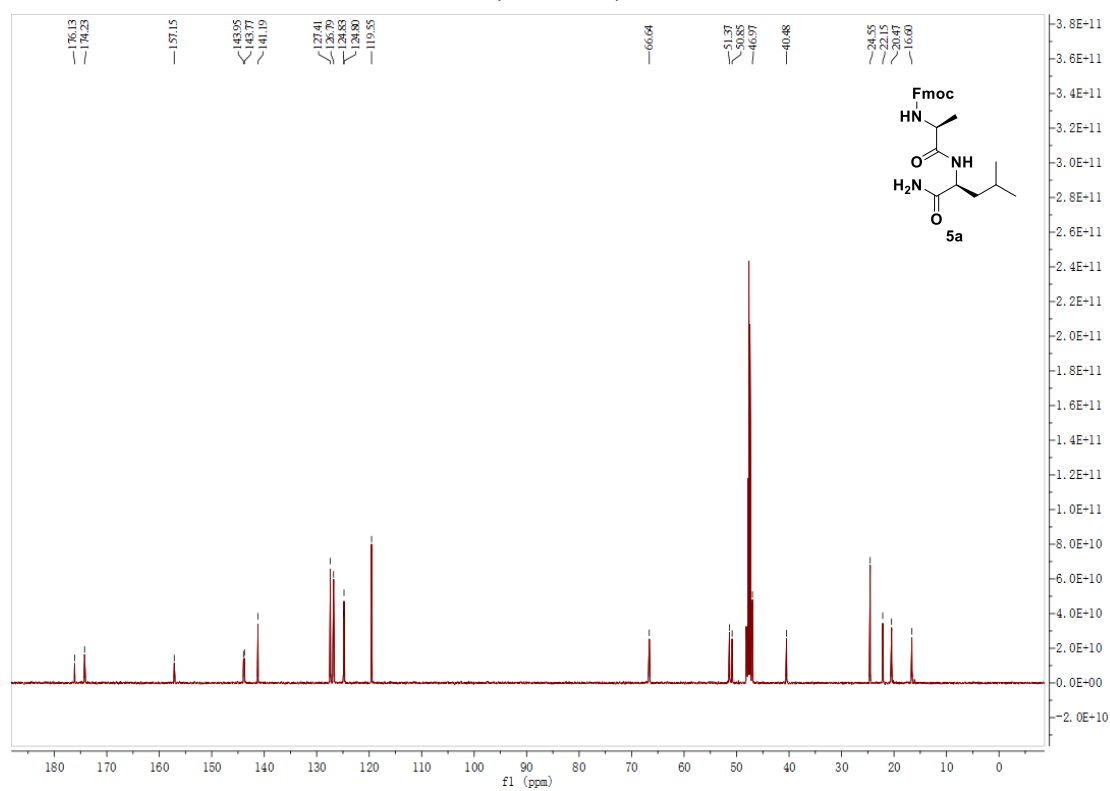
125 MHz, CDCl₃, ¹³C NMR



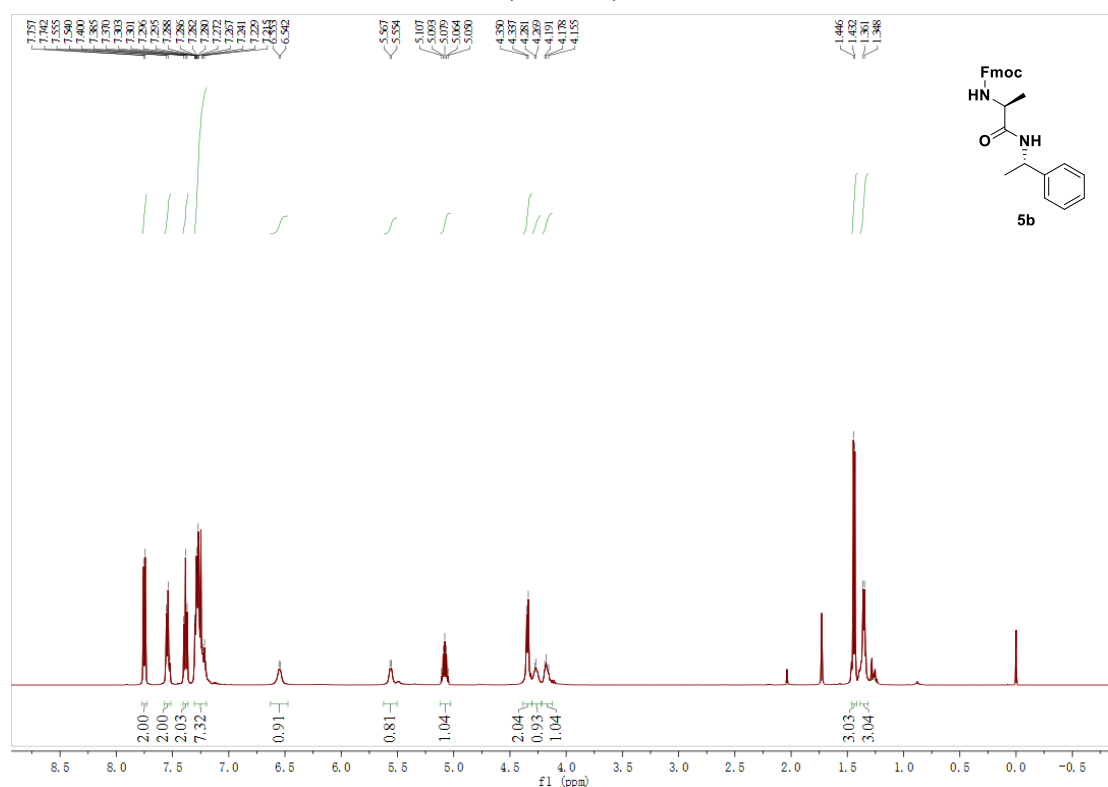
500 MHz, CD₃OD, ¹H NMR



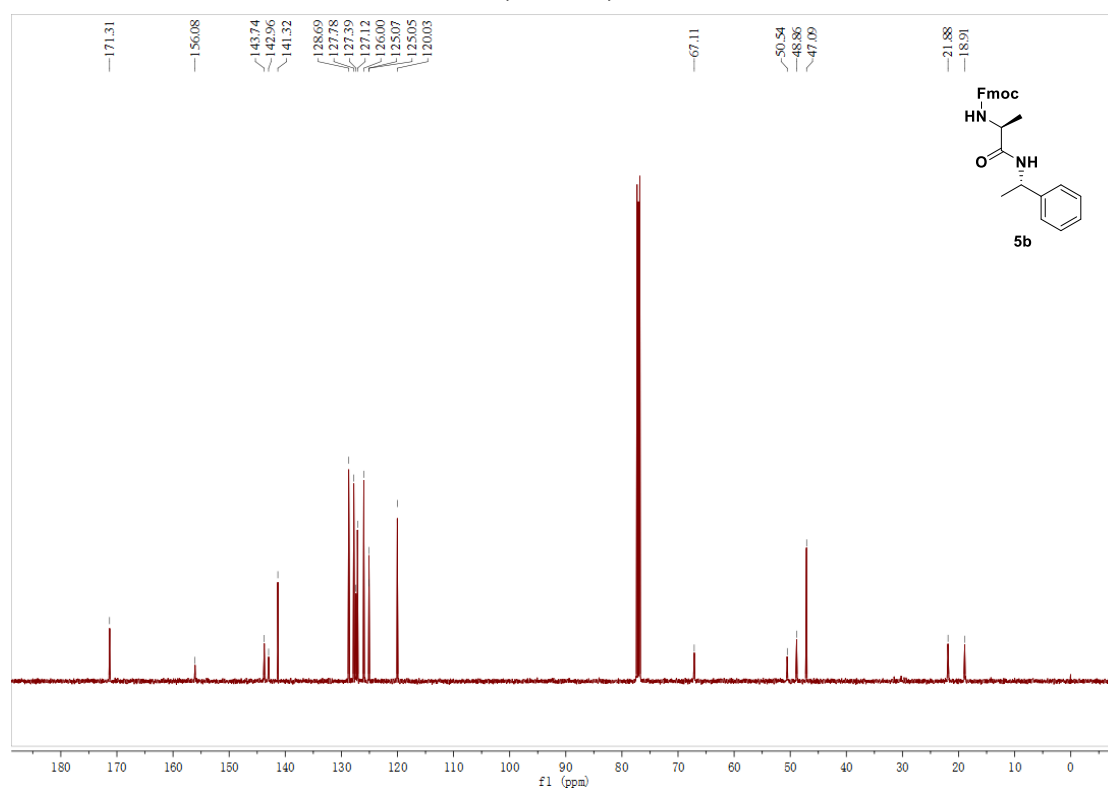
125 MHz, CD₃OD, ¹³C NMR



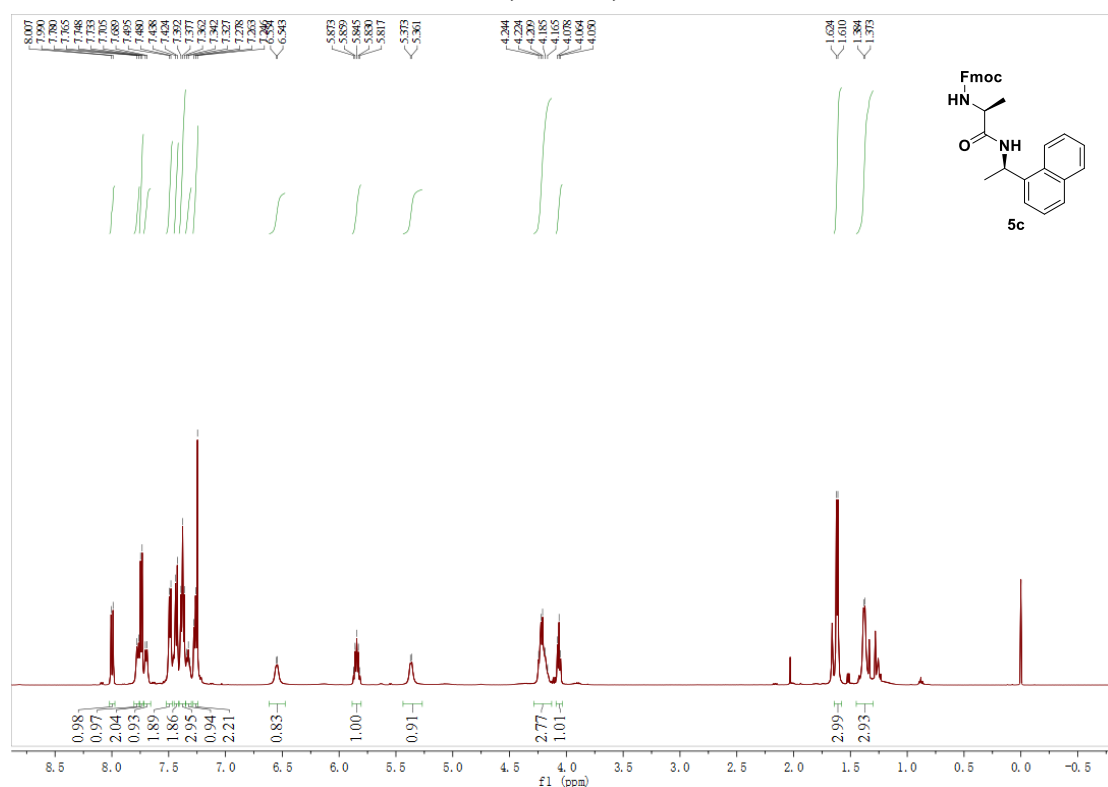
500 MHz, CDCl₃, ¹H NMR



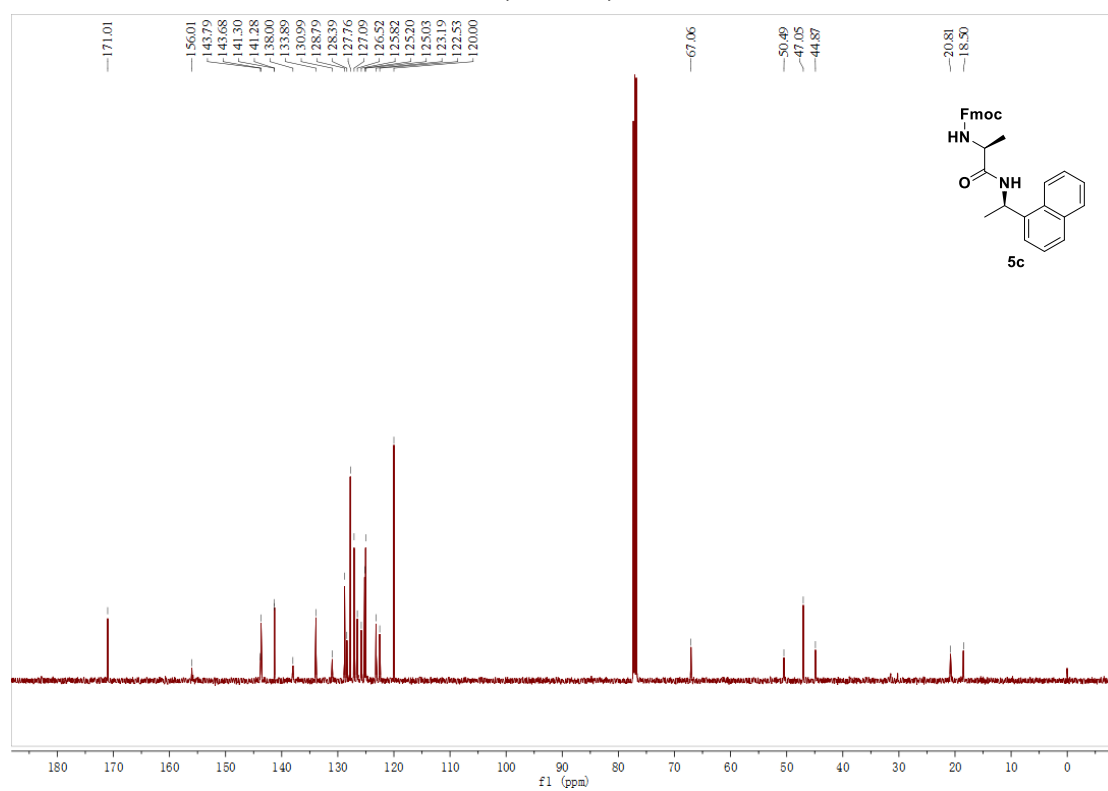
125 MHz, CDCl₃, ¹³C NMR



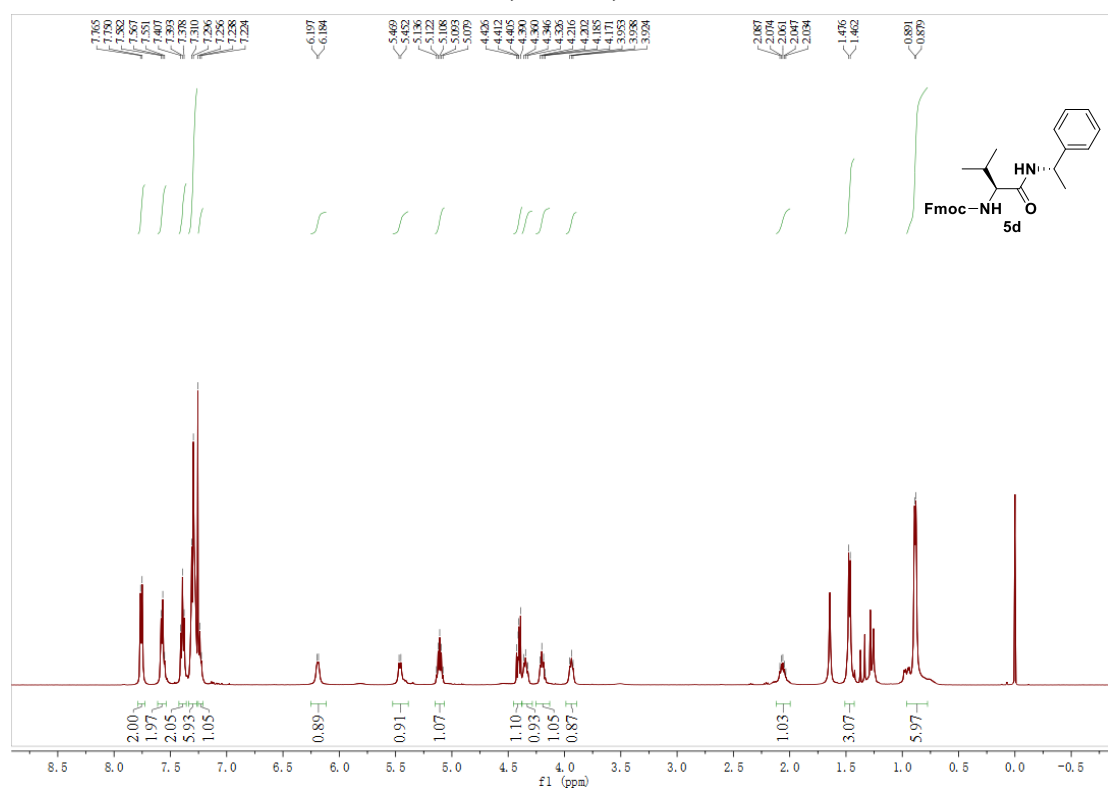
500 MHz, CDCl₃, ¹H NMR



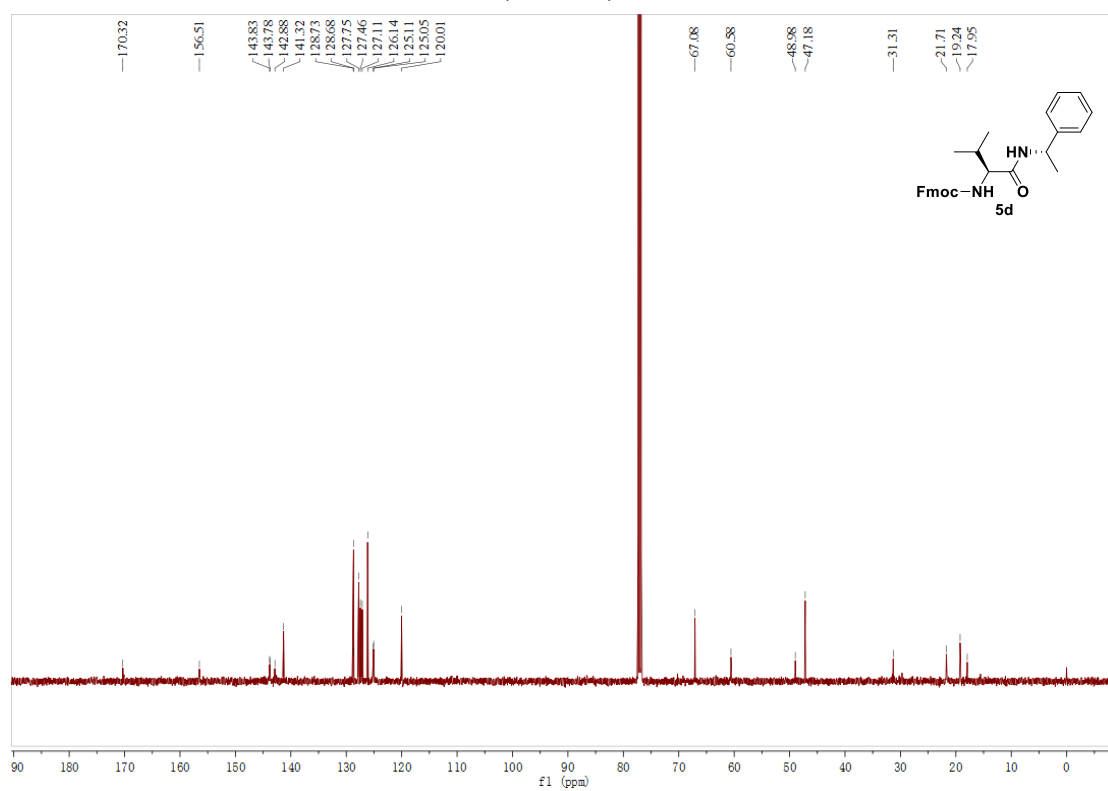
125 MHz, CDCl₃, ¹³C NMR



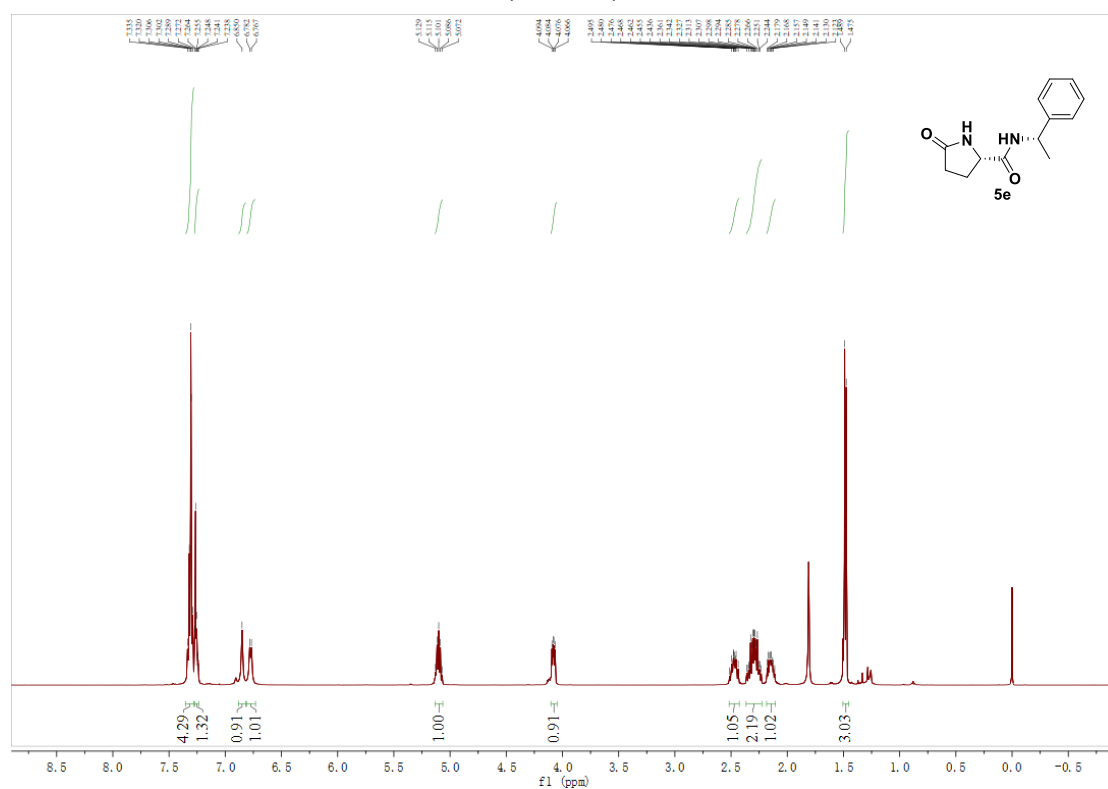
500 MHz, CDCl₃, ¹H NMR



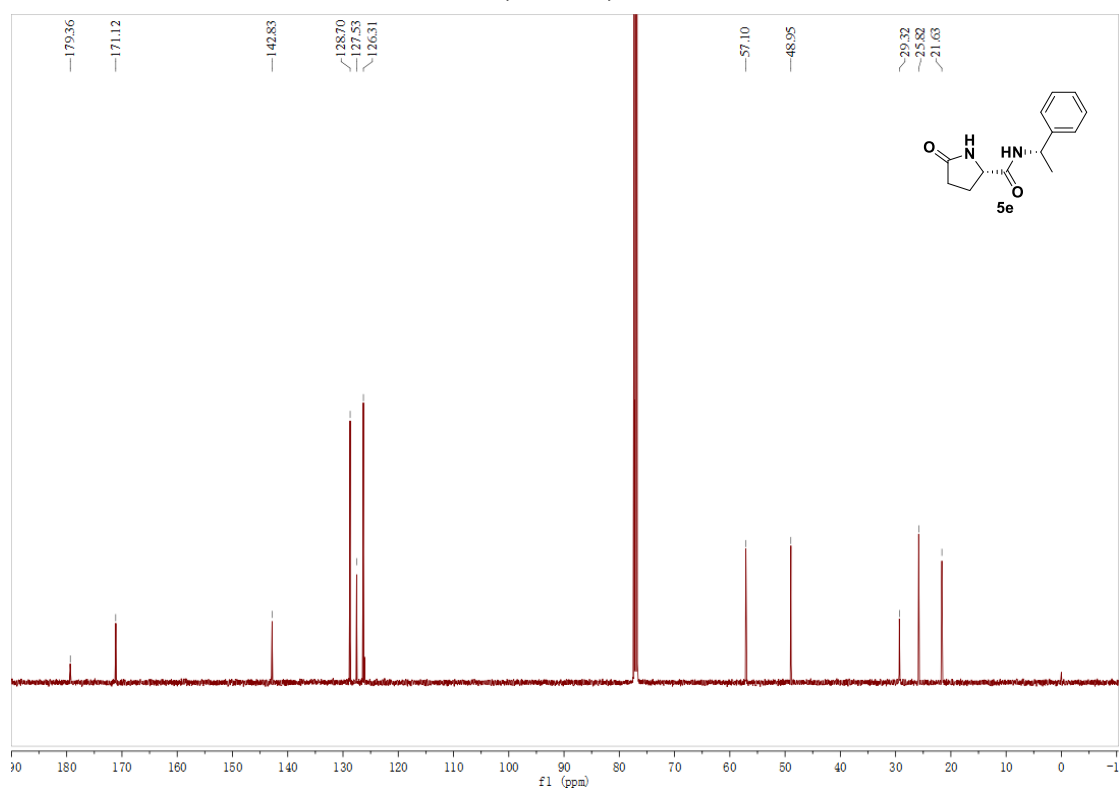
125 MHz, CDCl₃, ¹³C NMR



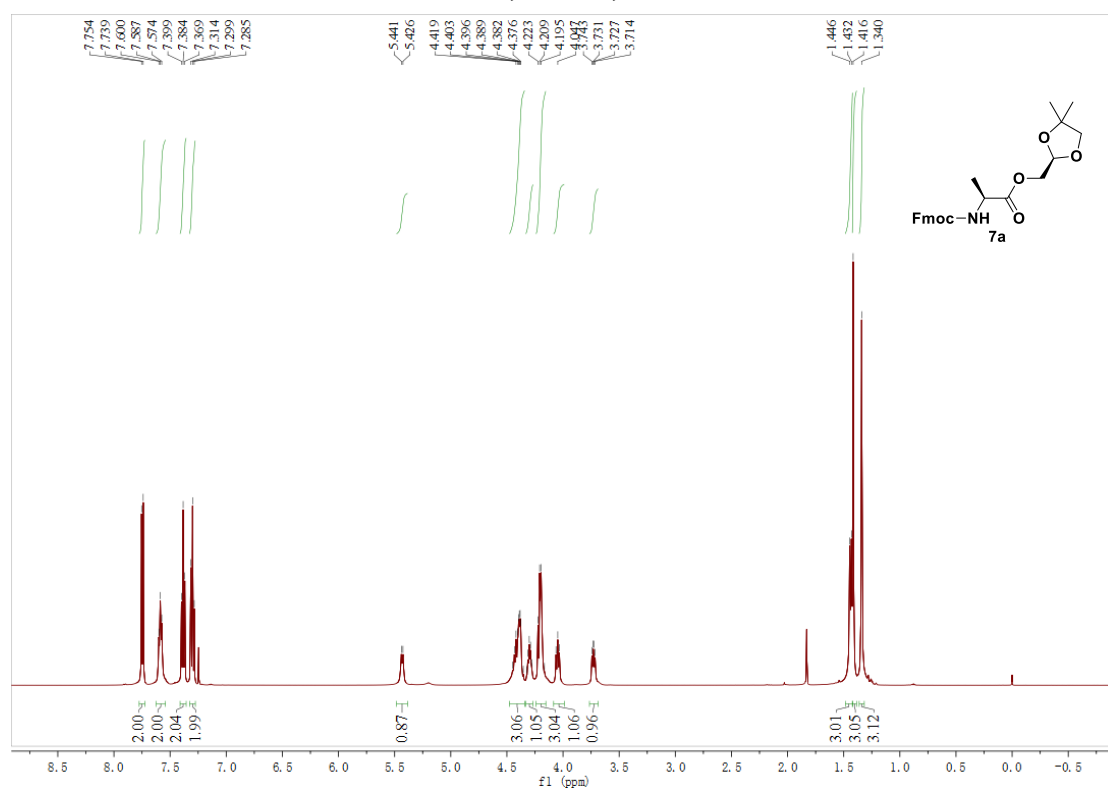
500 MHz, CDCl₃, ¹H NMR



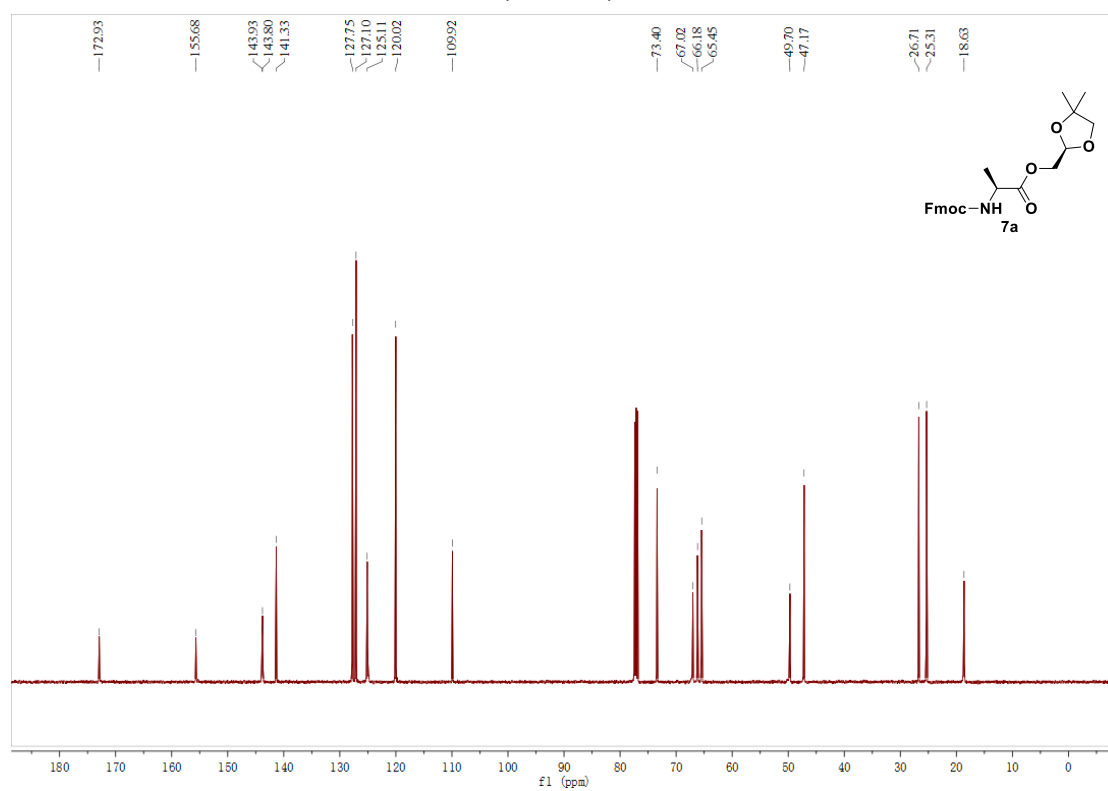
125 MHz, CDCl₃, ¹³C NMR



500 MHz, CDCl₃, ¹H NMR



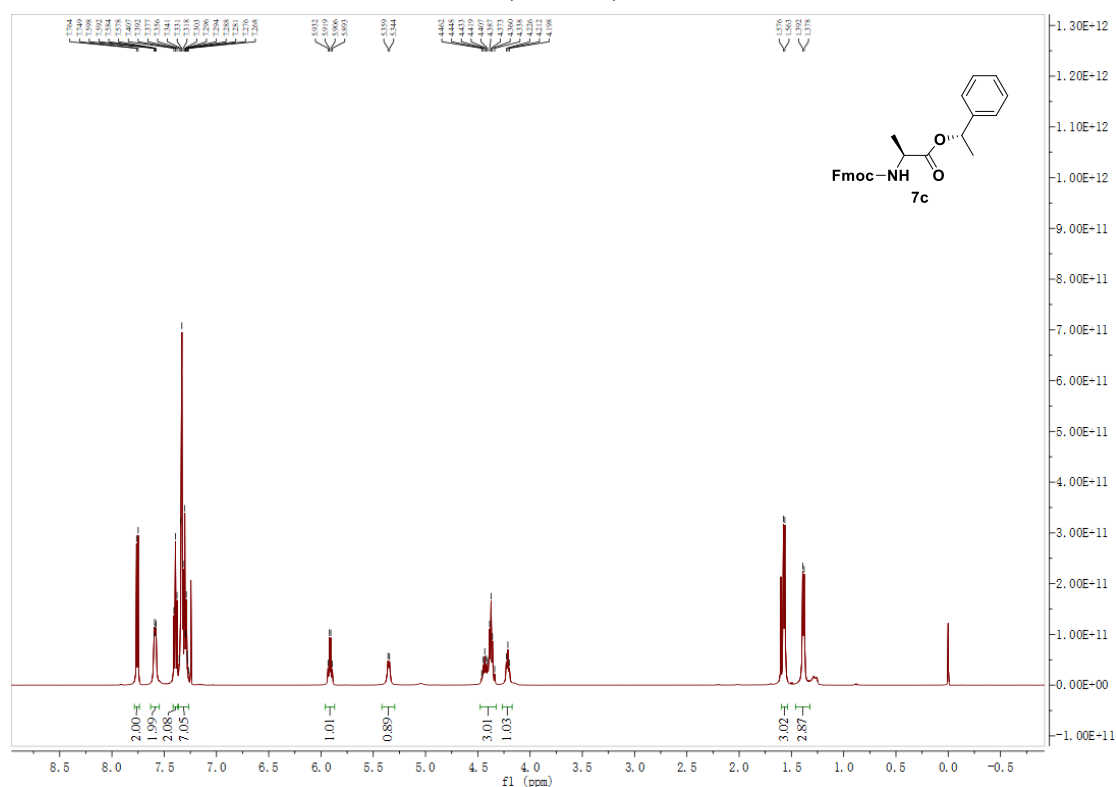
125 MHz, CDCl₃, ¹³C NMR



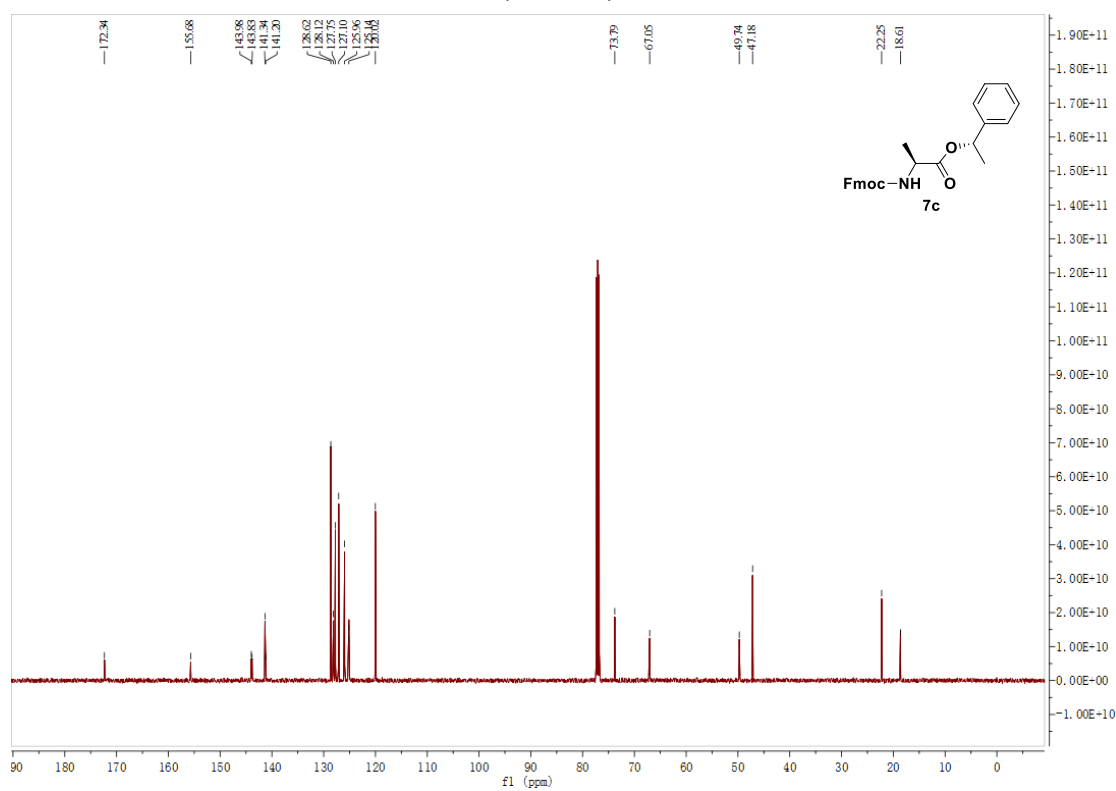
Chemical structure of compound 7b is shown in the top right corner of the spectrum.

Chemical structure of **7b** is shown in the top right corner of the spectrum.

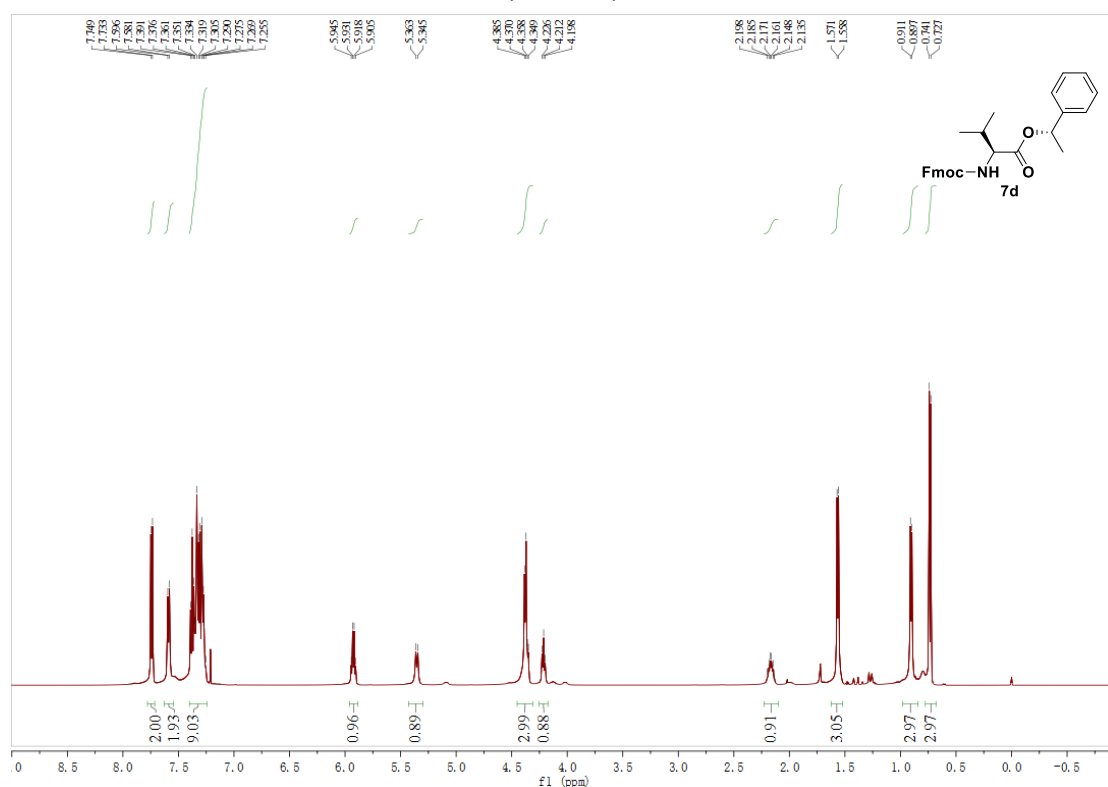
500 MHz, CDCl₃, ¹H NMR



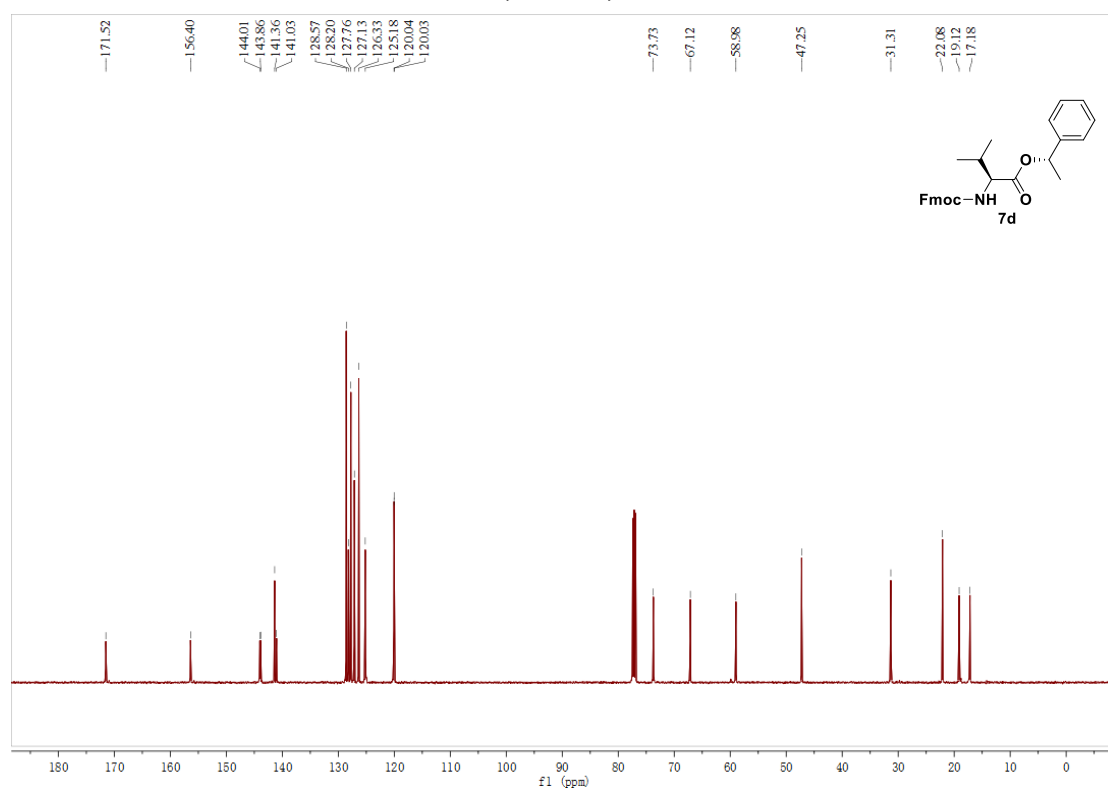
125 MHz, CDCl₃, ¹³C NMR



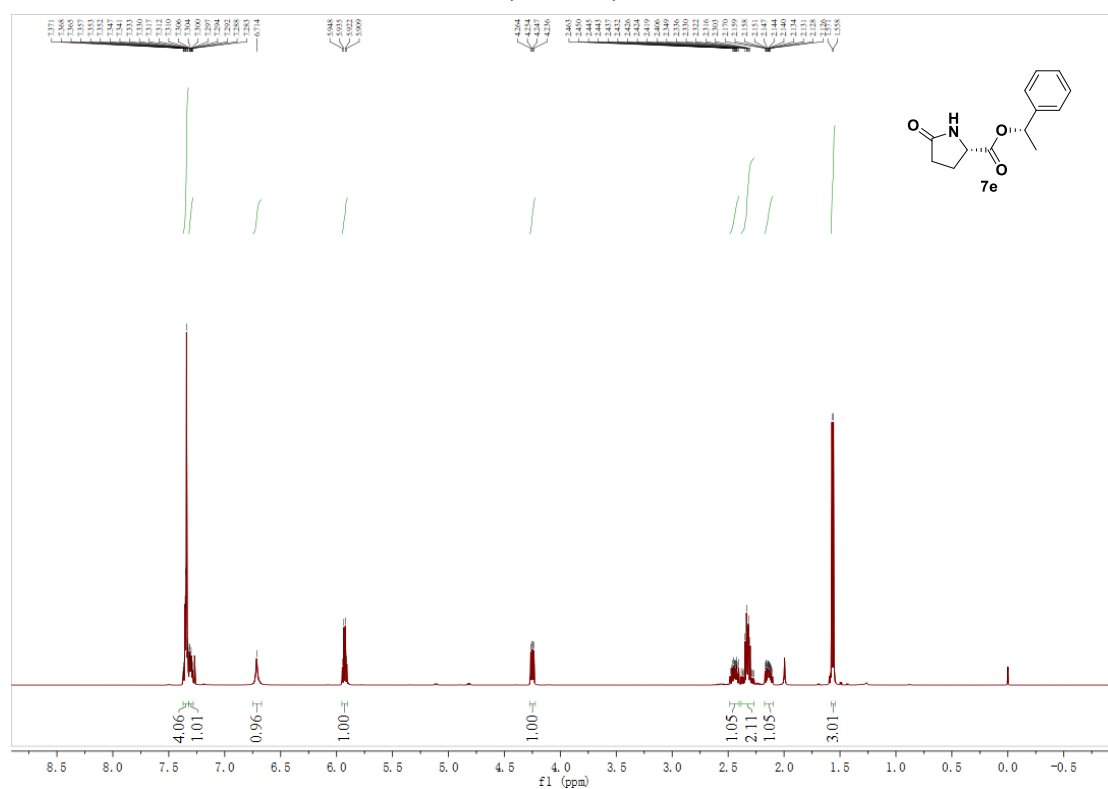
500 MHz, CDCl₃, ¹H NMR



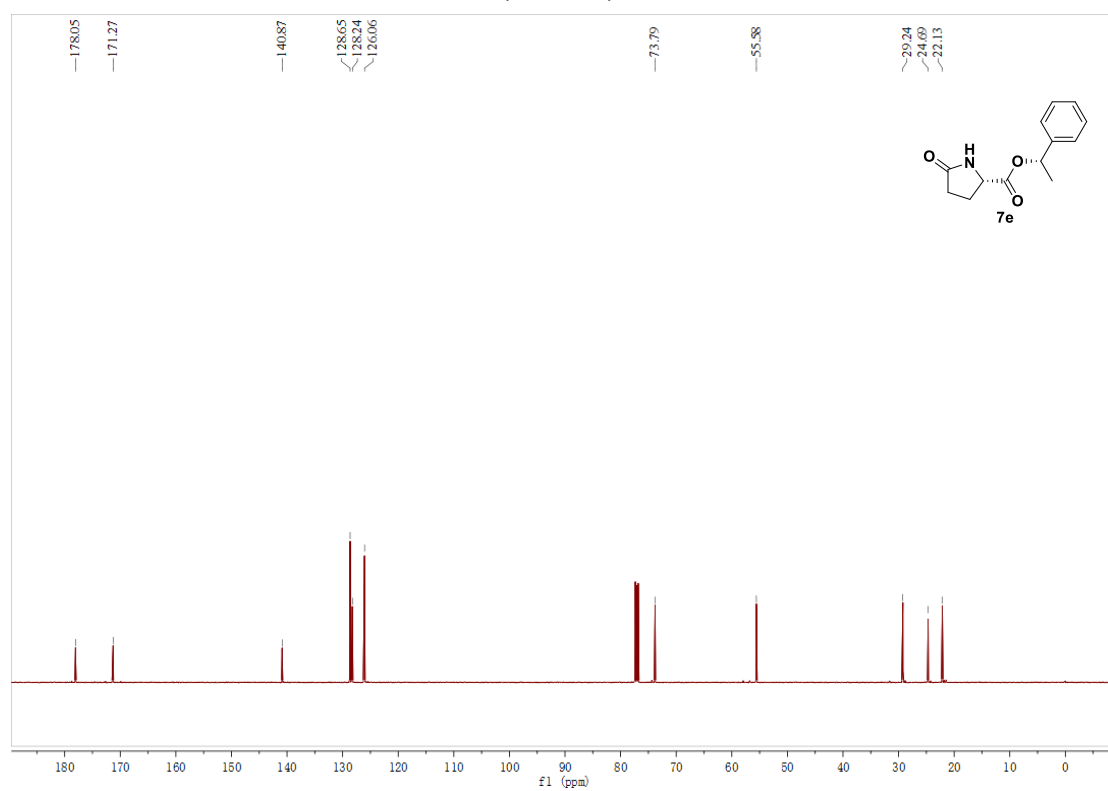
125 MHz, CDCl₃, ¹³C NMR



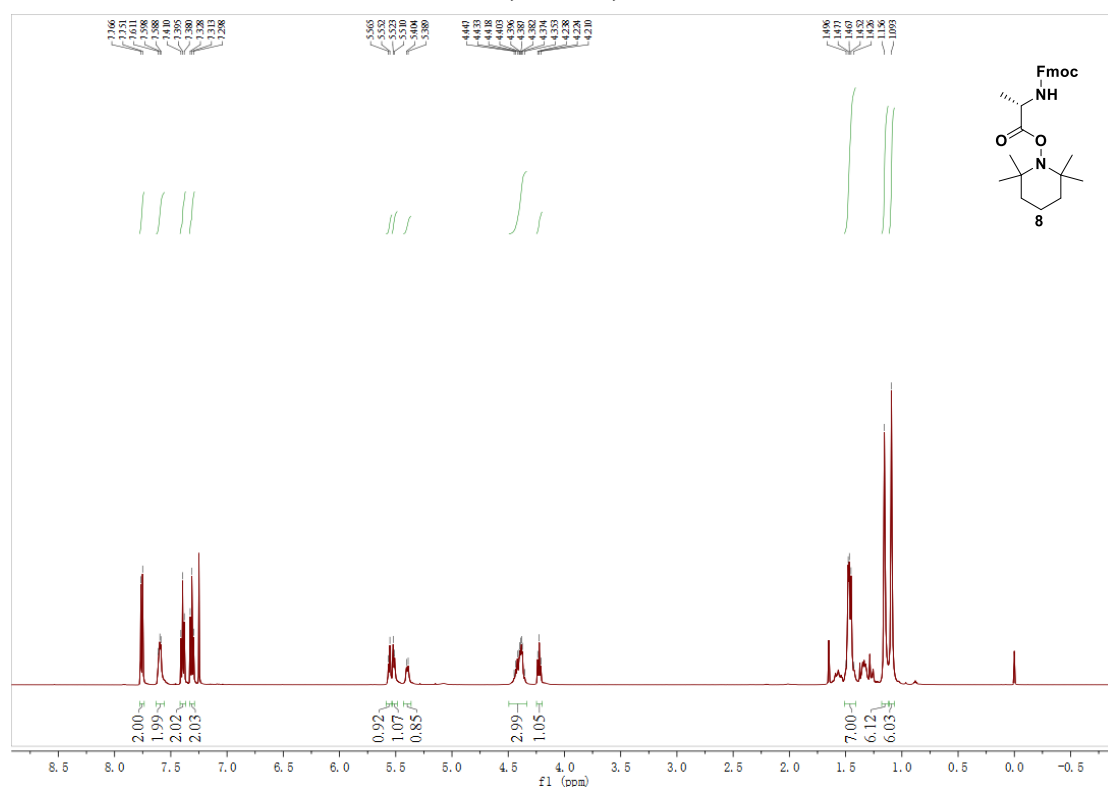
500 MHz, CDCl₃, ¹H NMR



125 MHz, CDCl₃, ¹³C NMR



500 MHz, CDCl₃, ¹H NMR



125 MHz, CDCl₃, ¹³C NMR

